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BRITISH COSMETIC CONGRESS

Manufacturing Chemist

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MANUFACTURING PERFUMER

Vol. XXX No. 4 A PUBLICATION OF THE LEONARD HILL TECHNICAL GROUP APRIL, 1959

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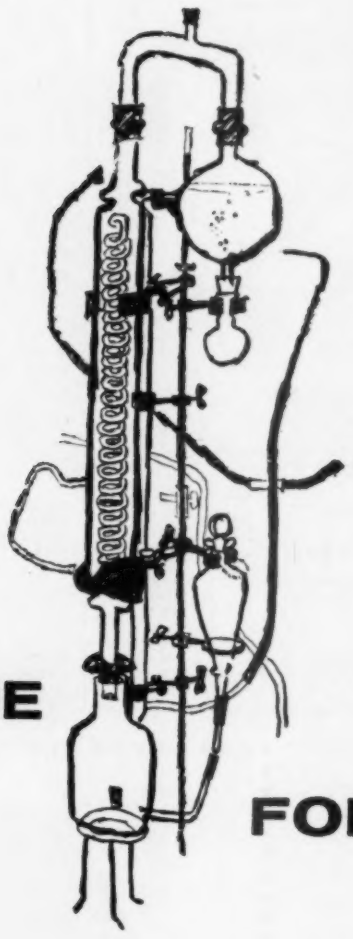

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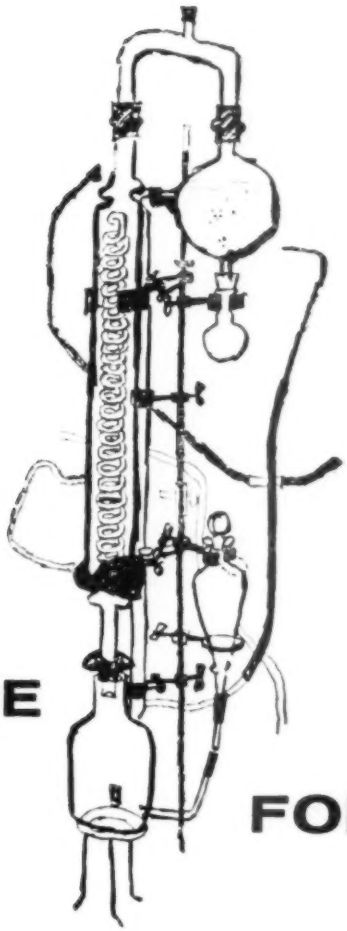

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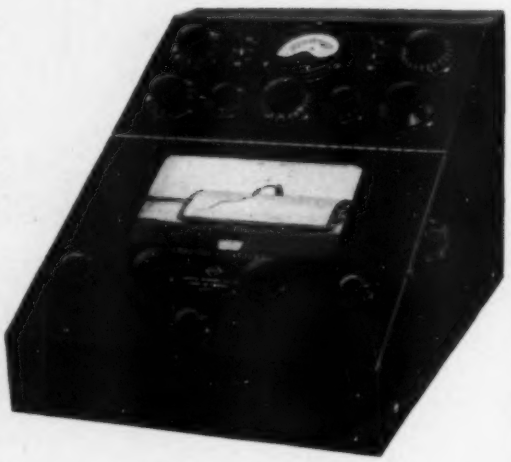

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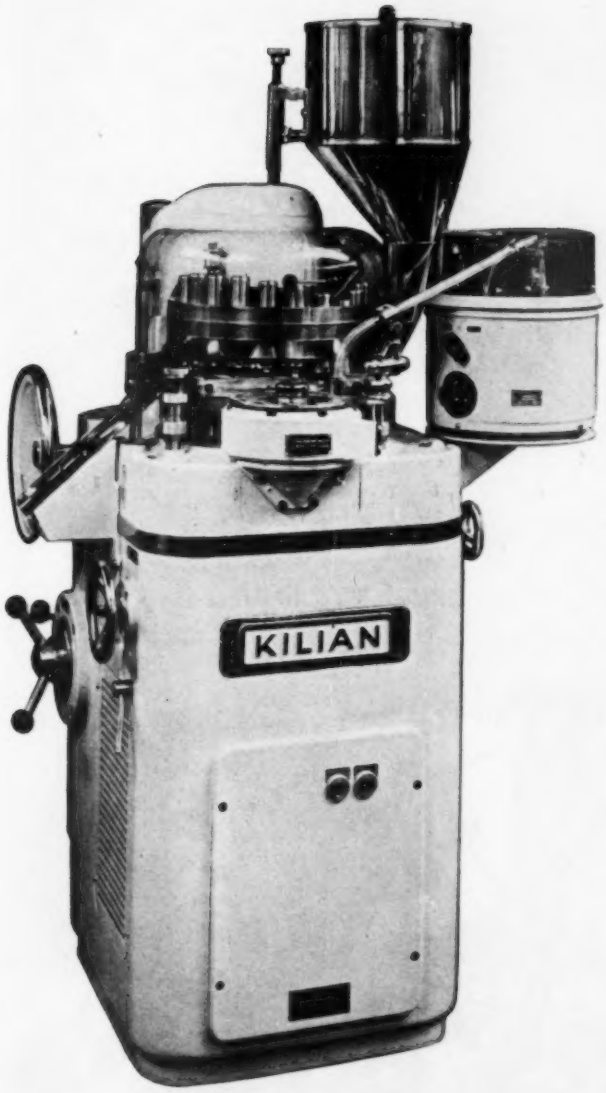

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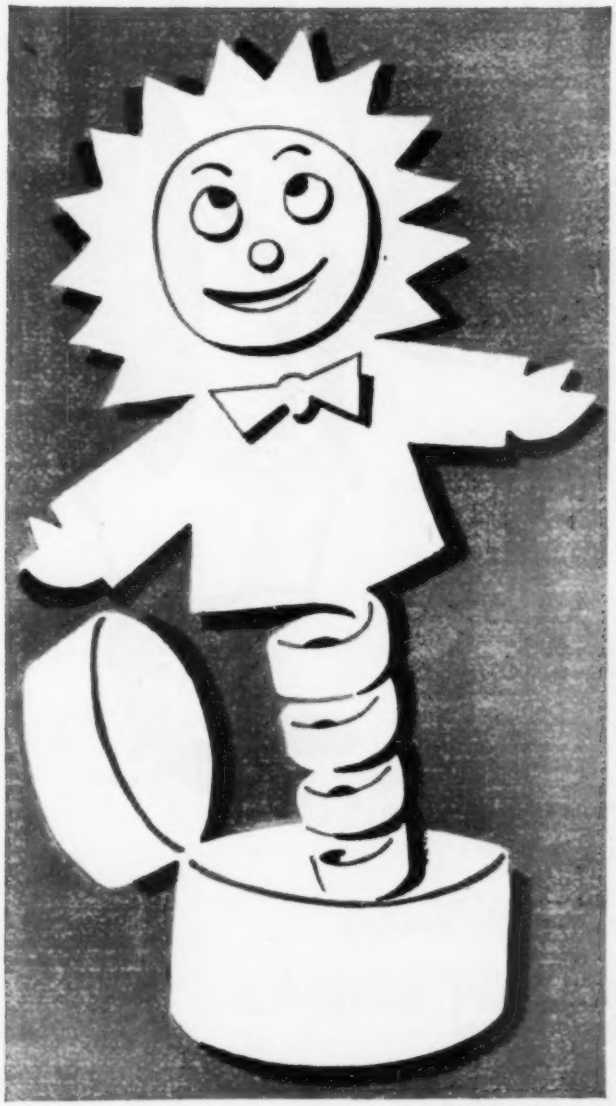

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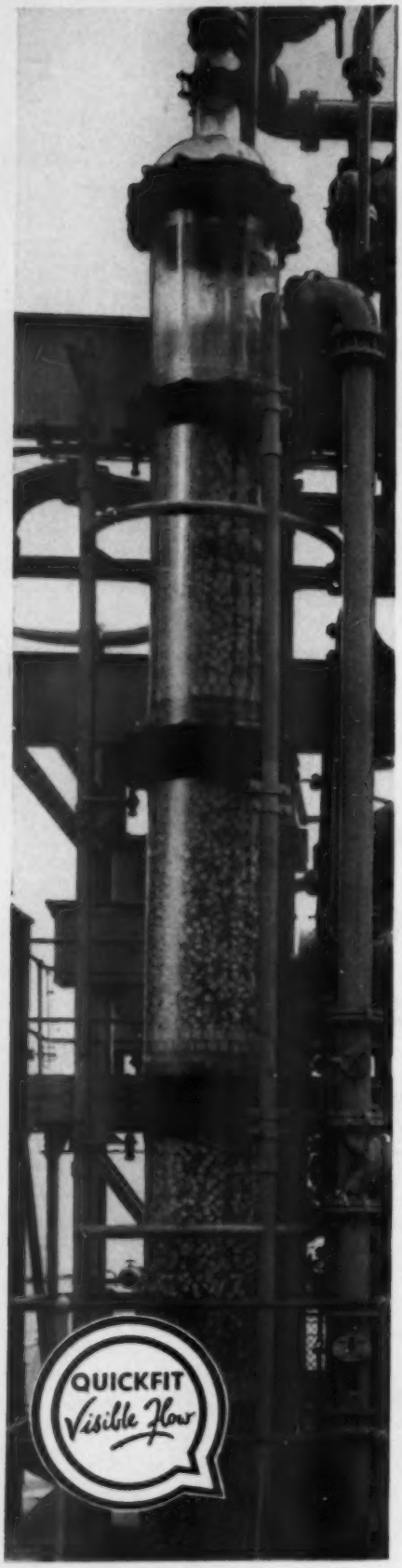

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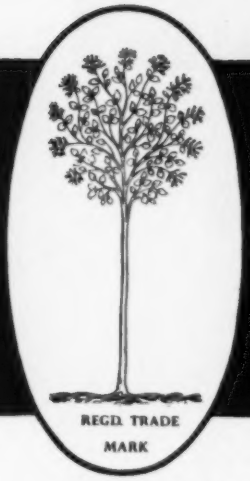

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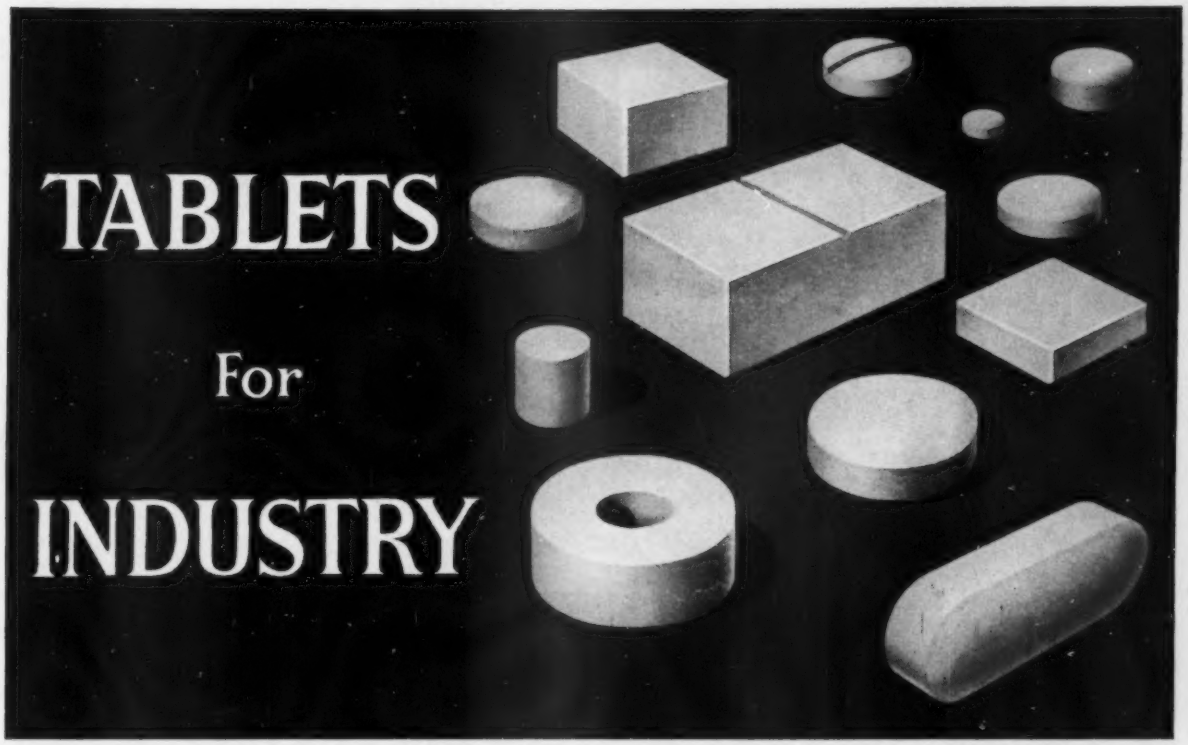

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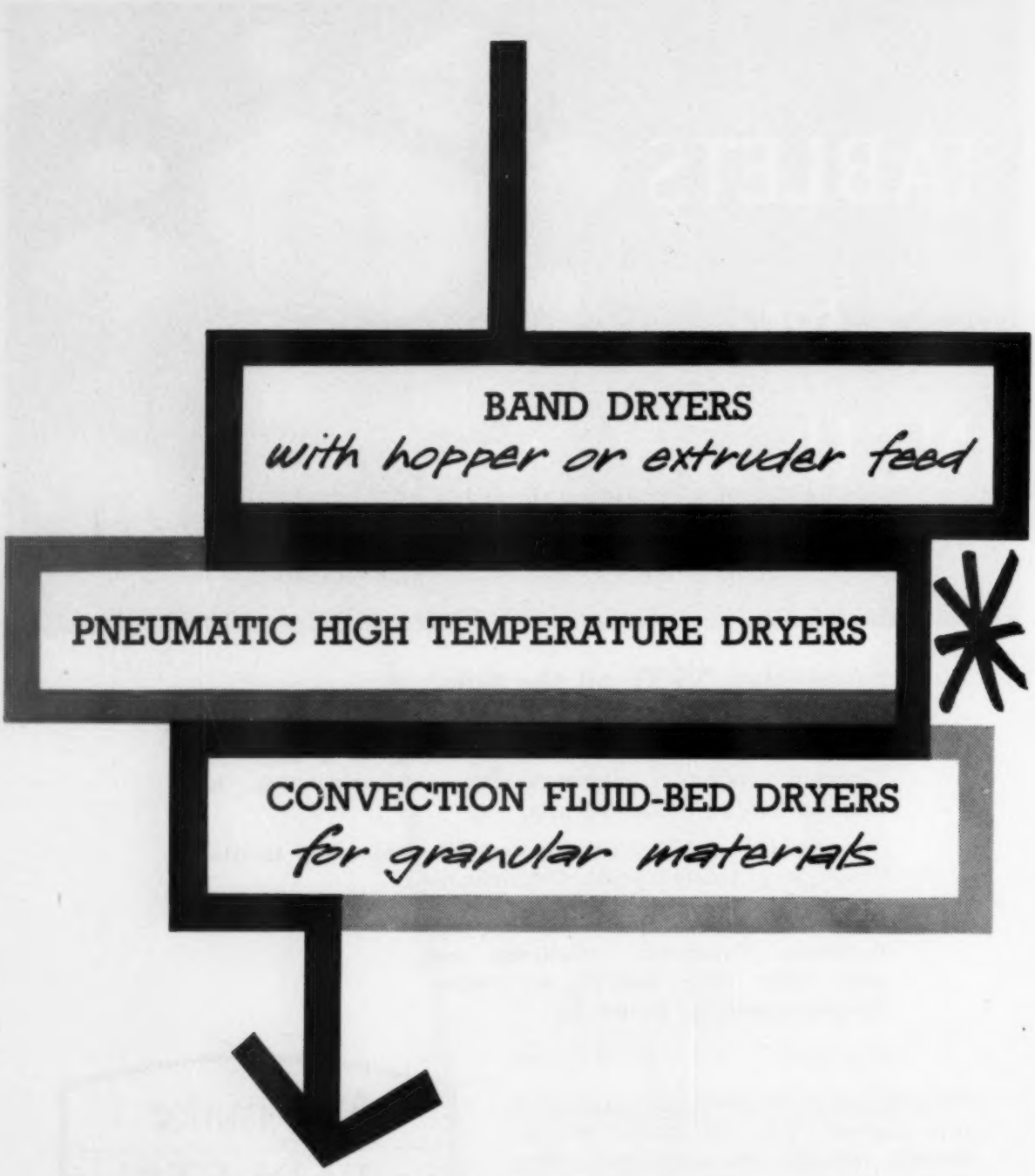

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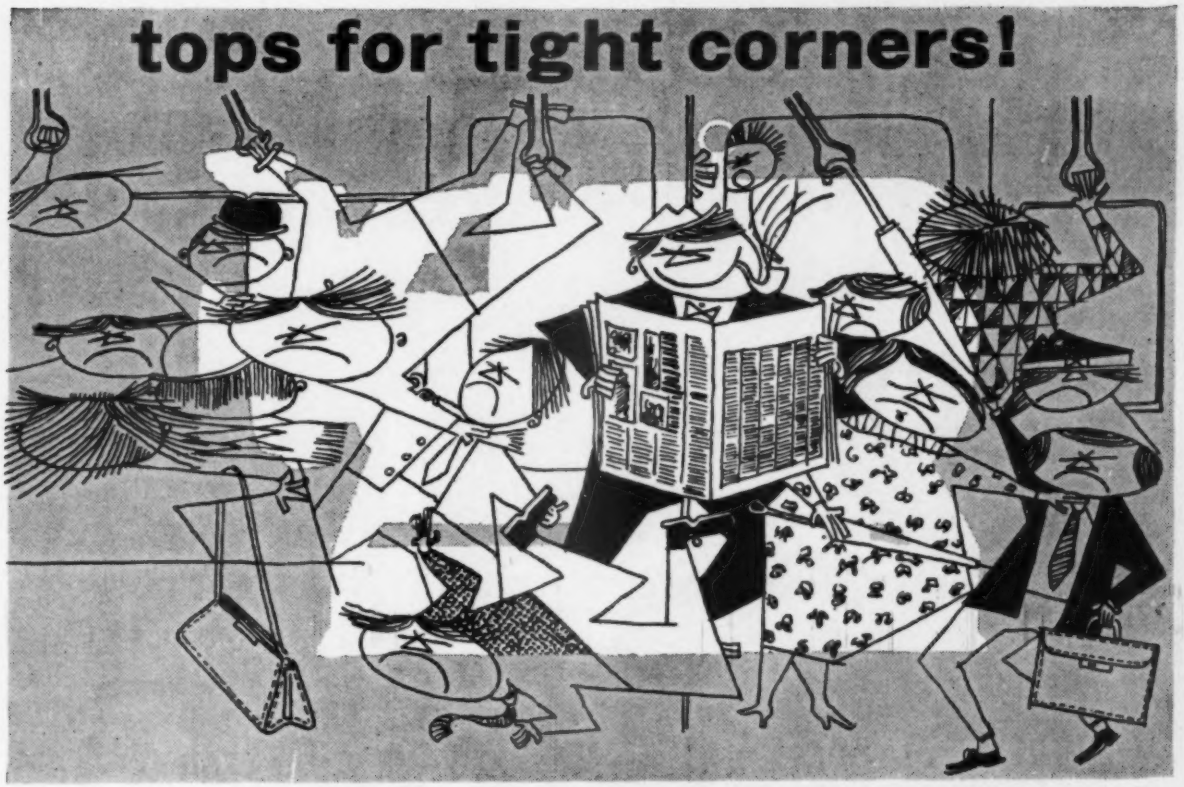

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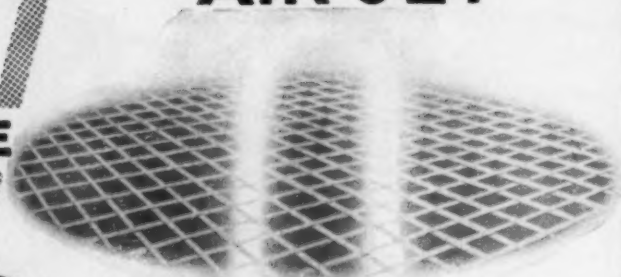

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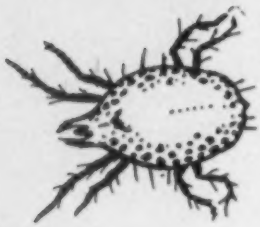

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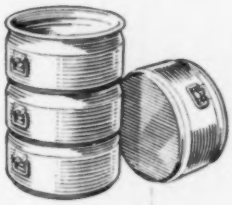

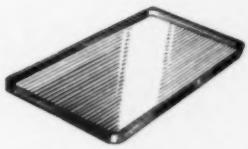

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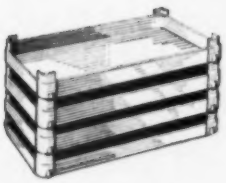

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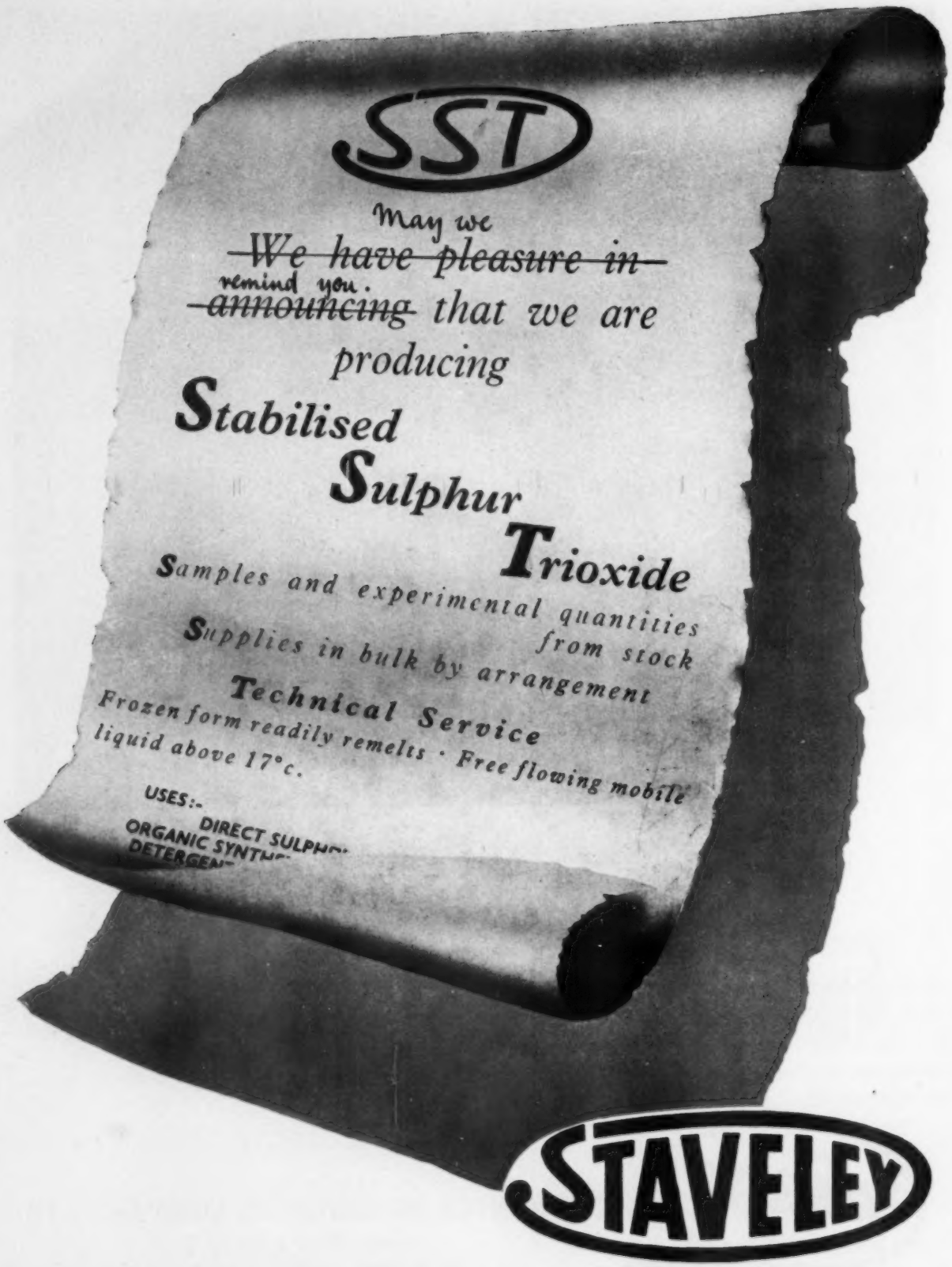

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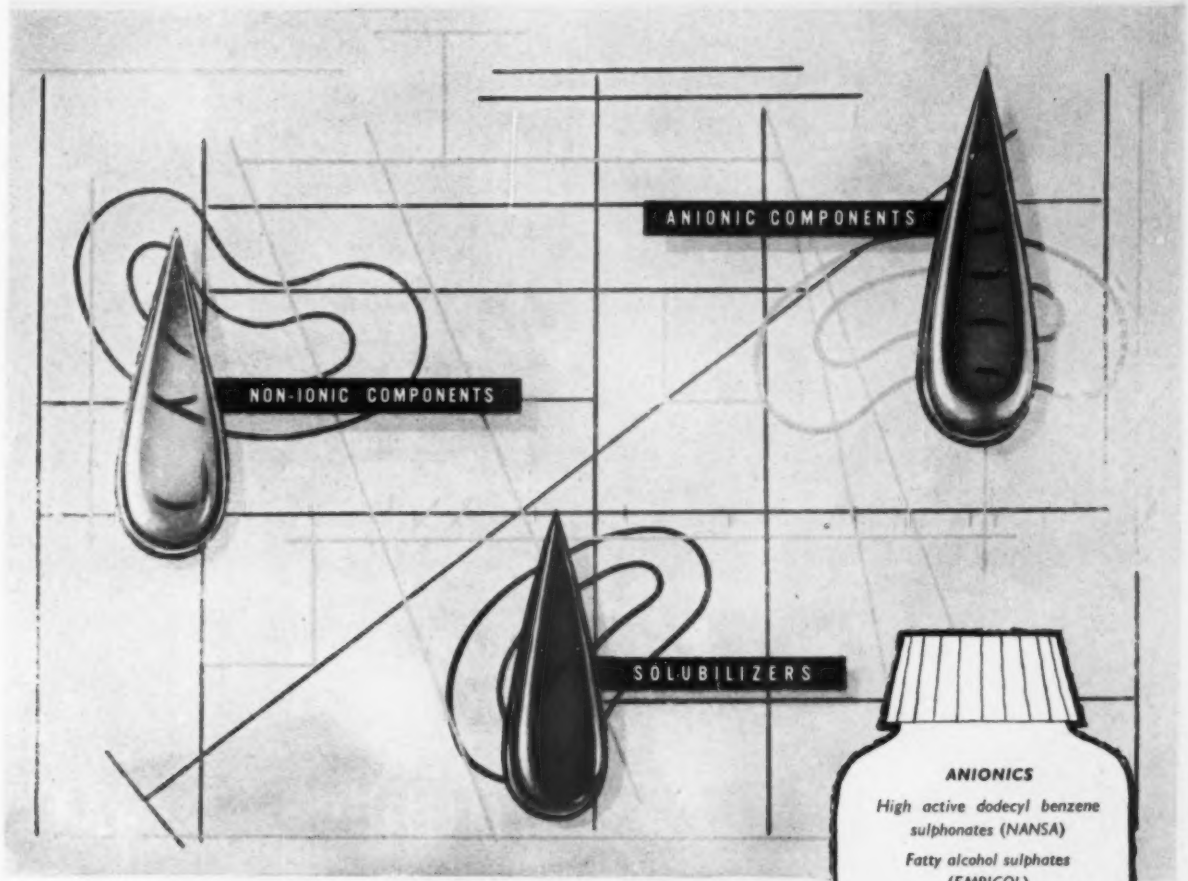

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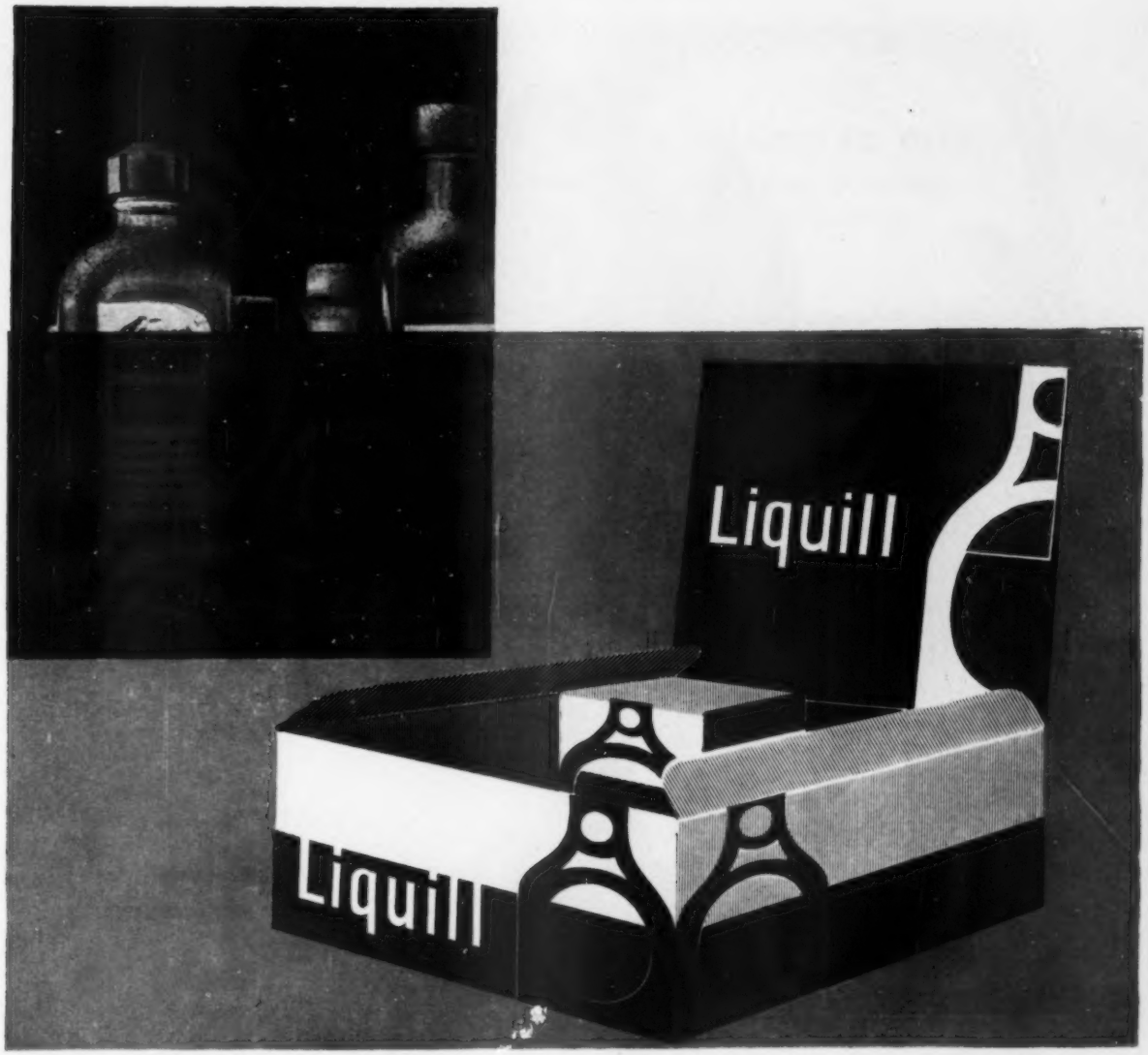

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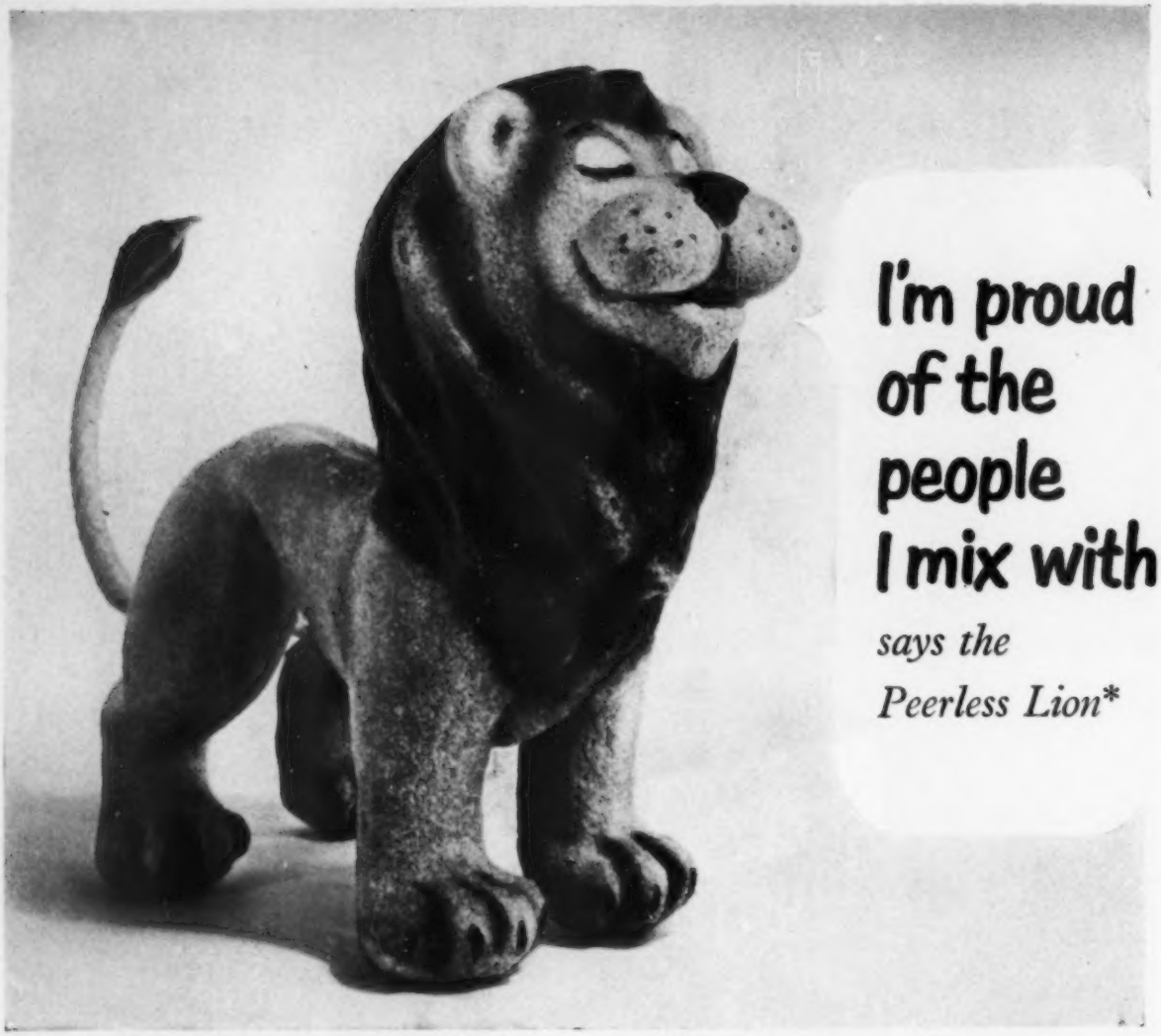

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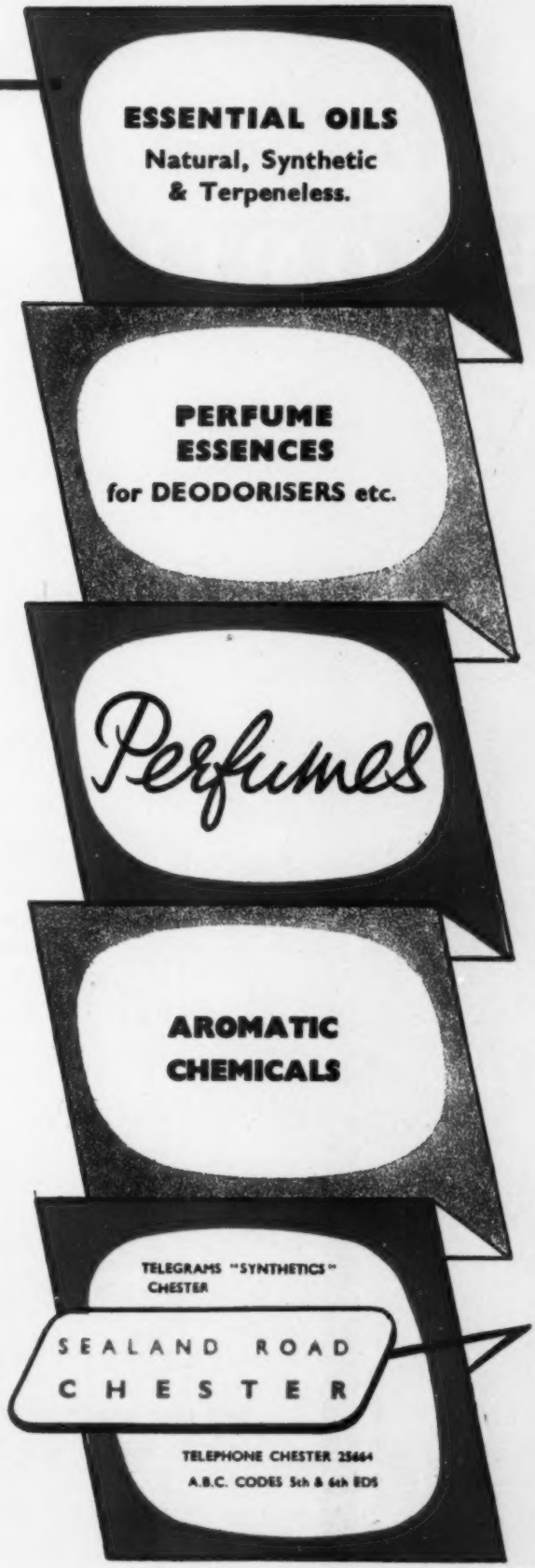

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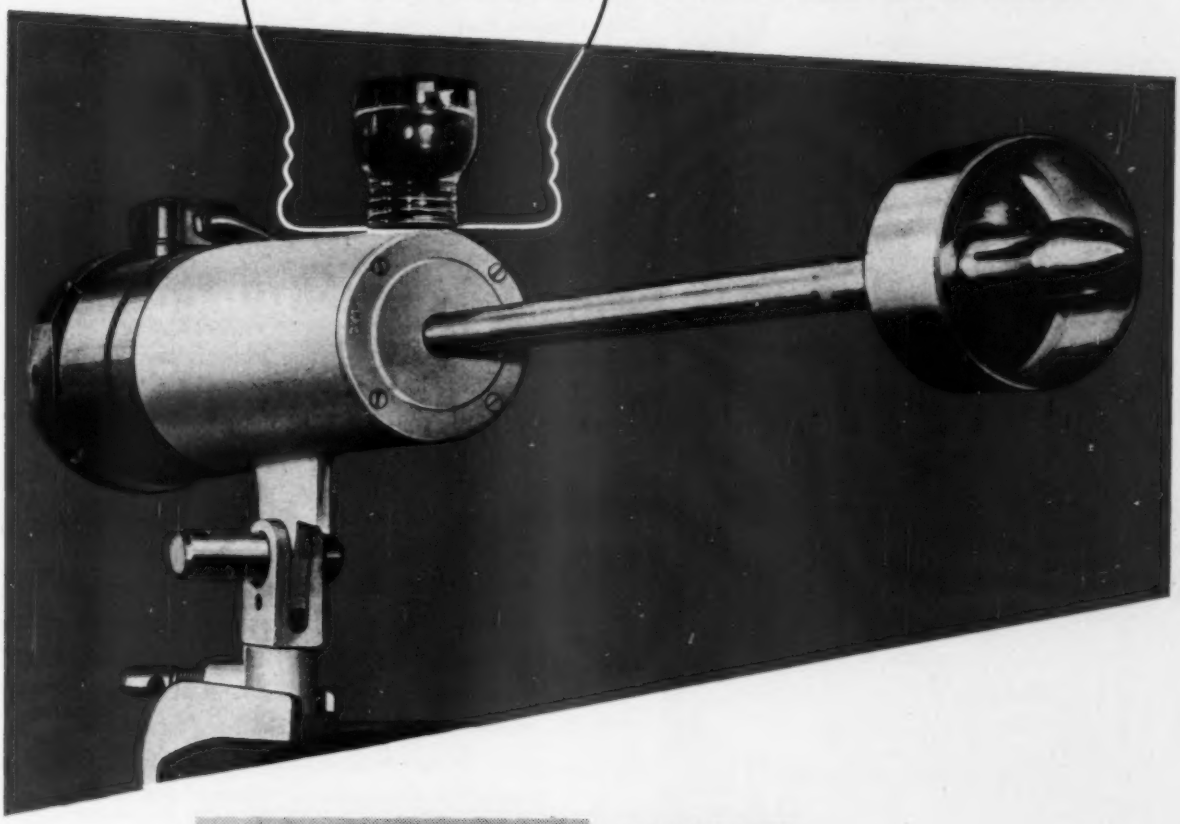

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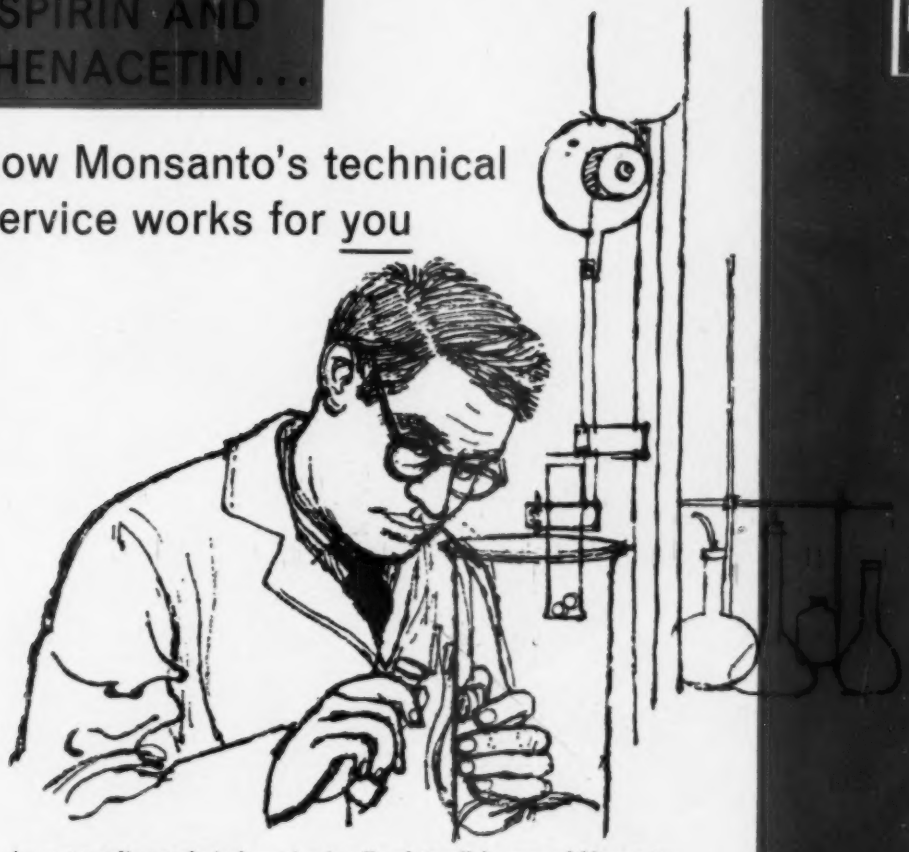
ASPIRIN AND PHENACETIN...

how Monsanto's technical service works for you



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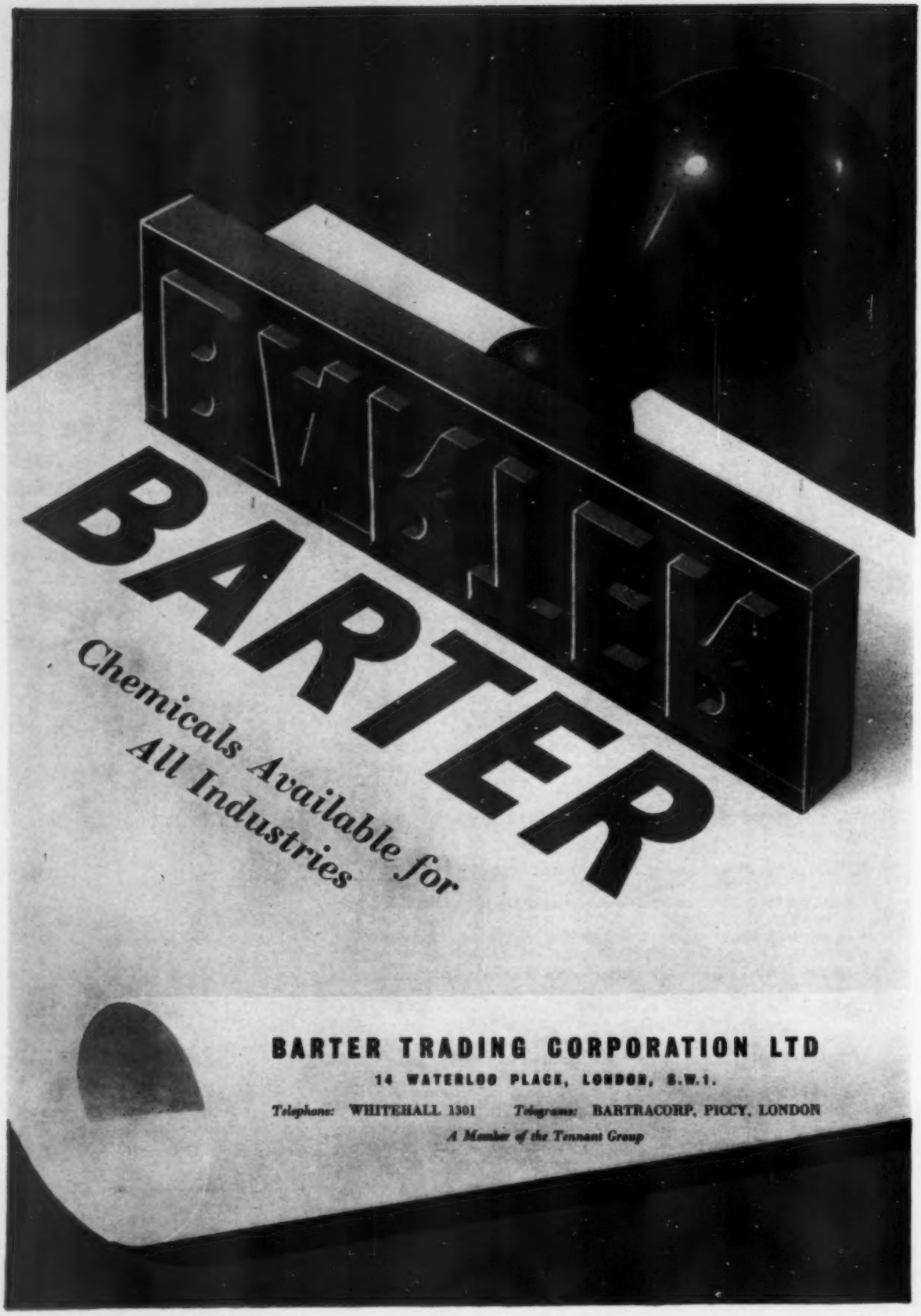
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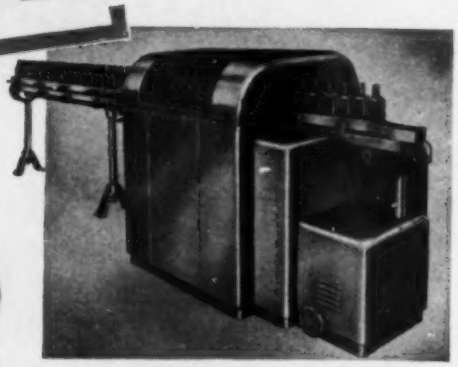

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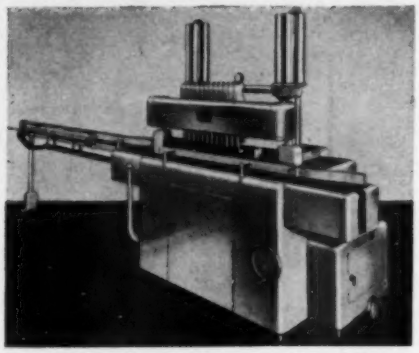

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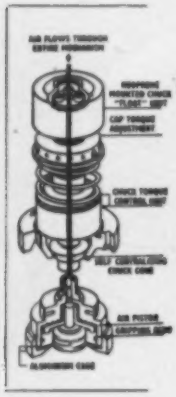

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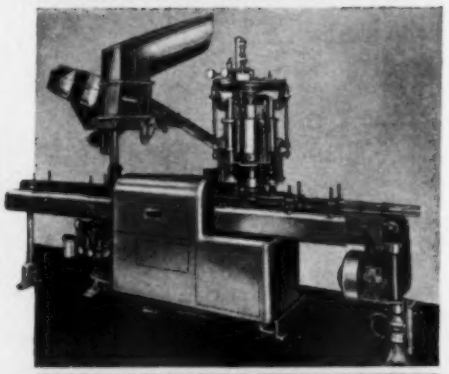

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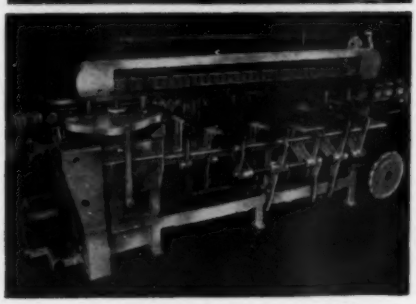

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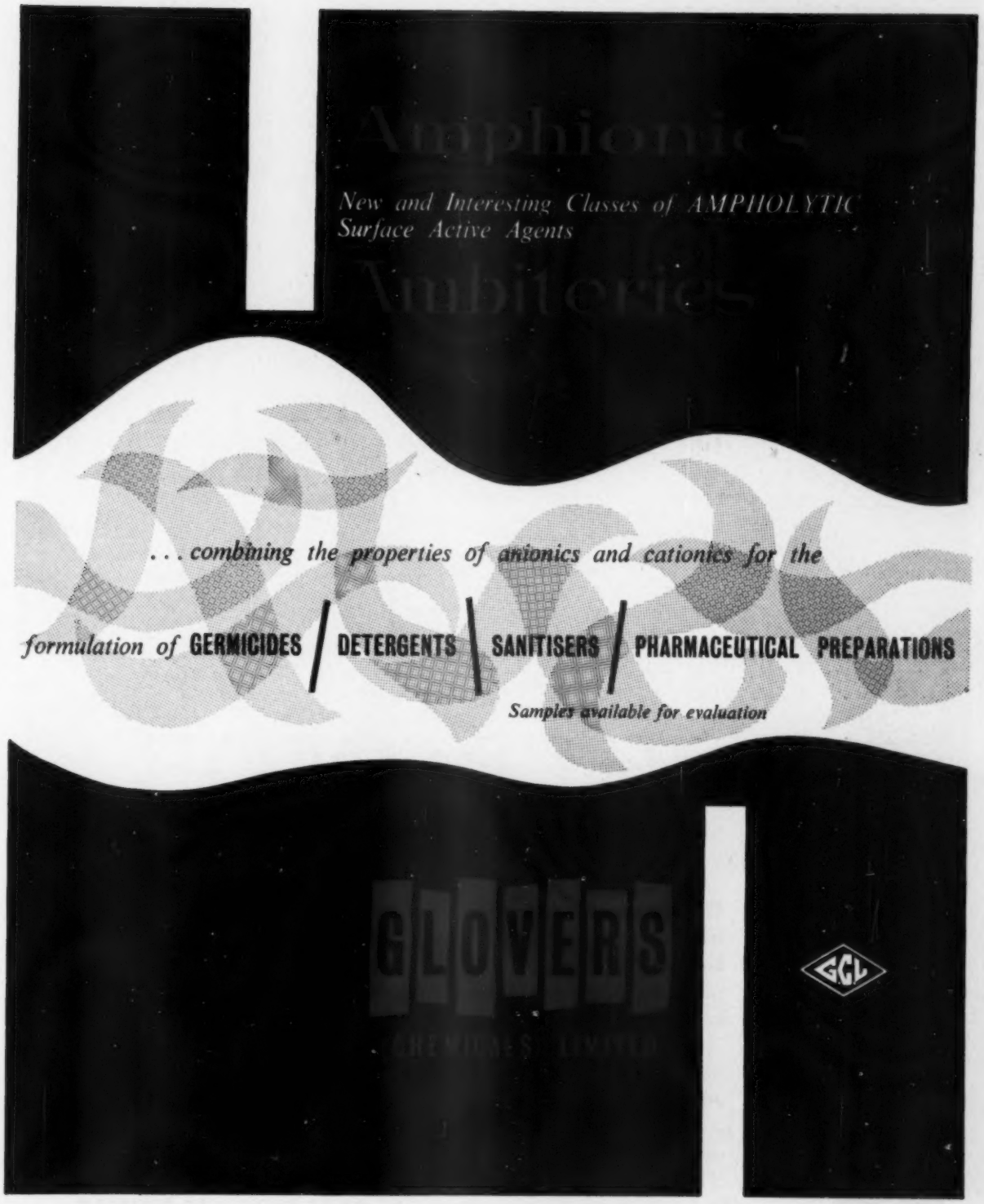
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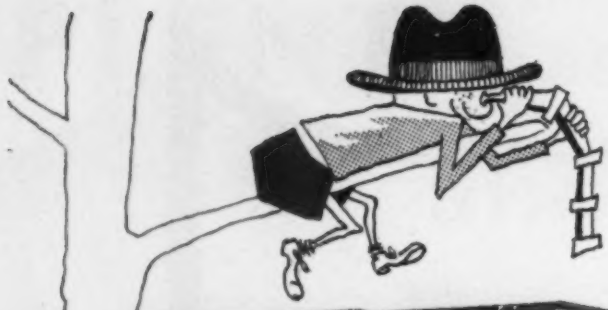

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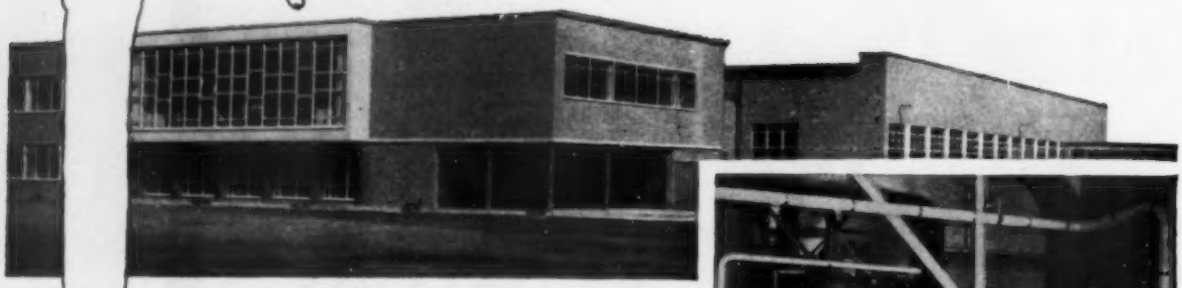
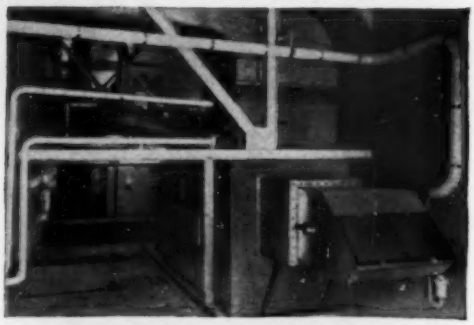


Creating the right atmosphere for antibiotics



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Manufacturing Chemist

Vol. XXX, No. 4 APRIL, 1959

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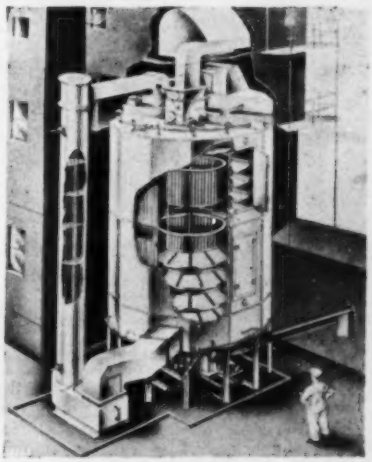

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TOPICS AND COMMENTS

Vaccines on the upswing

IN TERMS of money invested, vaccine manufacture appears to be the fastest growing section of the British pharmaceutical industry. In the past four years three firms have between them invested a sum approaching £4 million in vaccine production. Polio vaccine naturally accounts for the greatest investment. Glaxo have invested about £350,000 in their production unit at Sefton Park. Wellcome have spent £640,000 on their laboratories at Beckenham. And now Pfizer have opened a £1 million plant at Sandwich, details of which are given in this issue. So polio vaccine alone accounts for £2 million of the total investment.

Of course Pfizer do not expect to confine themselves to polio vaccine. Their large plant is obviously capable of making other vaccines and antisera. They have entered the vaccine industry because they correctly assume that biologicals are important for a large, broadly-based company and they have chosen polio vaccine for a start not only because there is a demand for it right now but because it gives their staff excellent experience which will serve them well when they choose to diversify.

Glaxo, of course, are already firmly established in biologicals. At the end of 1956 they opened Europe's only mass-production unit for BCG vaccine at Greenford. The laboratories cost £400,000 and provide facilities for making ærobic and anærobic vaccines as well as BCG. There are also virus, veterinary, microbiological and histopathological research units.

Meanwhile the Wellcome Research Laboratories at Langley Park, Beckenham, have been engaged on a massive programme of expansion for the past four years. They are investing no less than £2 million—mainly on new buildings for vaccines and antisera. Wellcome are determined to maintain their position as the leading manufacturers of biologicals in the British Commonwealth, a position based on manufacturing experience in the field dating back to 1894. The first unit of the five-year plan to be opened was the polio vaccine laboratories. Now three more buildings are in occupation. Two are similar in size and design to the polio vaccine laboratories, so now there are three new buildings at Beckenham devoted to research, development and production of medical and veterinary virus vaccines. The total floor area is 75,000 sq. ft. and the capital cost about £700,000. The fourth new building is a 30,000 sq. ft., two-storey structure for anærobic vaccine manufacture. It cost £300,000. The third and final phase of the Beckenham development is now under construction and is due for completion early next year. In it will be produced antisera and prophylactics for medical and veterinary use. The cost of the building follows the average at Beckenham of £10 per sq. ft.

The combined efforts of Glaxo, Wellcome and Pfizer over the past four years have immensely strengthened and enlarged the British vaccine industry. Clearly we can expect continuous development in this field, particularly in virus vaccines. A lot of work is being done on influenza vaccines. Then there is interferon, with its novel effects upon viruses. Looking further ahead, is it likely that the next step in cancer therapy may be a vaccine? Whatever the future holds British vaccine manufacturers seem to be in good fettle to take full advantage of every development in this exciting field.

Truth about cosmetics

THAT the first British Congress of Cosmetic Science, due to open at University College, London, on April 15, will be stimulating and instructive is very clear from the pre-prints of the papers which are reviewed elsewhere in this issue. Apparently the members of the Society of Cosmetic Chemists of Great Britain voted on the subjects for the Congress and it seems they will be getting their money's worth from the authors of the 16 papers.

The authors mix instruction with criticism—some of it unpalatable. Dr. W. S. Bullough, of the University of London, is extremely outspoken in his paper which is somewhat deceptively entitled "The Present State of the Cosmetic Industry." The industry, he complains, is dispensing treatment for a living organ, the skin, yet it has little or no conception of the problems really involved. He concedes that better creams, lotions and powders now on the market are triumphs for cosmetic chemists, but he argues that the true science of cosmetics does not lie in the more perfect production of pleasing chemical mixtures. "It lies in the skin itself. The face is not an old boot to which it is logical to apply a fine cream of dubbin, or a fine polish of wax; it is a living organ which makes the most complex demands on the blood and which depends on the proper functioning of the most involved metabolic processes. And like the rest of the body it is subject to ageing, which is to say it is subject to an increasingly severe deformation of those metabolic processes."

But where is the industry to get advice on the requirements of the skin? Can dermatologists help? Hardly, because of course, they are concerned with abnormal skins, not normal ones. So when it comes to the subject that matters most to the cosmetic

chemist—the normal skin—medical advice is useless. Dr. Bullough's answer is that the industry should itself conduct research on the skin, if necessary by joint action. Frankly this is a counsel of perfection. We cannot see how such a highly competitive industry could agree to finance research of this kind. This is not to say that it is not highly desirable. If the industry is ever to take itself seriously a research programme on these lines is the essential first step.

It will be extremely interesting to listen to the discussion on Dr. Bullough's paper. Mr. D. H. Powers' paper on laboratory tests of products contains some equally arresting views. Papers of this calibre can do much to persuade the industry to face its responsibilities. For these alone the Congress will have been well worth while.

Proprietaries reclassified

THE classification of proprietary medicines into six numbered categories for guiding doctors in their prescribing has given rise to the widespread belief that the categories denote a decreasing order of therapeutic merit. This, of course, is quite wrong. For example, category 1 (preparations of proved value but not yet standard) and category 8 (standard preparations, and new remedies of proved value, in elegant form or vehicle) might well be of equal therapeutic merit.

To remove these serious misunderstandings the Standing Joint Committee on the classification of proprietary preparations (the Cohen committee) has reclassified proprietaries into lettered instead of numbered categories.* The revised categories are:

N—New drugs of proved value which are not yet "standard" (*i.e.* described in the British Pharmacopœia, British Pharmaceutical Codex and British National Formulary).

S—(*a*) All preparations whose active therapeutic constituents are identical with or modifications of those of "standard" preparations;
(*b*) elegant preparations of drugs in Category N;
(*c*) mixture of drugs in Category N with drugs in Category S.

P—Preparations which are not "standard" for which *prima facie* evidence of therapeutic value is presented, but which the Committee cannot accept as of proved therapeutic value without further evidence, which must be provided within a period stipulated by the Committee.

O—Preparations not "standard" which in the Committee's view have not been proved of therapeutic value.

H—Preparations which are a combination of drugs in category O with those in categories N, S. or P.

The letters are themselves an *aide mémoire;* N=New drugs, S=Standard drugs, P=Postponed judgment, O=Not of proved therapeutic value; and H=Heterogeneous—mixture of O with other categories.

The Committee advise that N and P preparations should be freely prescribable, that S should be prescribable under certain conditions, and that practitioners should be discouraged from prescribing those in categories O and H. At the same time they say "there should be no absolute restriction on the prescribing by a general practitioner of any drug which in his opinion was necessary for the treatment of his patients."

P is a new category of "suspended judgment" in which a new drug not yet standard, but for which there is *prima facie* evidence of value, could be placed for a specified period during which the manufacturer would be asked to provide conclusive evidence of its value. At the end of this specified period (unless the Committee otherwise determine) if the evidence is not presented the drug will be categorised as "not proved of therapeutic value."

But during the period of "suspended judgment" the drug should be prescribable without the prescriber being called upon to justify his prescription. For example, if it is claimed that drug "X" will arrest or cure cancer of the stomach even in a relatively few patients, and the *prima facie* evidence presented with the claim is suggestive, the Committee consider that it would clearly be wrong to withhold the drug until its value had been conclusively confirmed or refuted.

The report has been circulated to all practitioners accompanied by a letter from Sir John Charles, Chief Medical Officer, Ministry of Health, in which he stresses that "you will doubtless wish to refrain from prescribing any preparation in these categories (O and H) unless you are satisfied that it is essential for the treatment of an individual patient."

* Classification of Proprietary Preparations Report of the Standing Joint Committee. H.M.S.O. 6d. net.

Revolution in the bathroom

ALTHOUGH our forefathers found nothing strange in men using perfume, and no doubt themselves used considerable quantities of empasms and preparations that "mitigateth the imposthume of the arm holes," as Albertus Magnus so neatly put it, during the last hundred years or so the use of scent by the stronger sex came to be looked upon as unmanly and ridiculous. However, within the last decade this outlook has changed and it is estimated that in Britain now some £500,000 is spent every month on toilet preparations for men. According to an article in *The Director*, sales of men's toilet preparations now amount to about one-tenth of the £65 million spent on cosmetics annually.

These greatly increased sales can be attributed to three main factors. First, to the overcoming of male prejudice against using anything scented; second, to a successful sales appeal to women, who usually introduce men to toilet preparations and who also buy about 50% of all male toilet products; and third, to the use of large displays of men's toilet preparations. It seems likely that the present trends in the sale of these products will continue; perhaps in a few years time men will be buying more than a third of all toilet preparations, as they now do in America.

Headaches for exporters

RUSSIA and China are likely to be the most serious competitors for British chemical exporters in the future. This is the view of Mr. S. P. Chambers, a deputy chairman of I.C.I. In a comprehensive and statistic-packed review of international competition in the chemical industry, given as the annual lecture of the Plastics Institute, Mr. Chambers put his finger on many of the political and economic problems that beset British exporters.

Europe is easily the largest export market for chemicals; it takes more than one-third of total free world chemical exports and it is expanding rapidly. But Britain is not doing nearly so well in this market as West Germany and the U.S. And the position certainly will not be helped by the creation of a European Economic Community with Britain on the outside.

If we find ourselves being ousted from the rich European market, where else can we turn? The U.S. seems to present a rich and reliable market—the penalty for too much success is likely to be swift and severe. The lobbies in Washington are immediately worked upon by interests affected by the overseas competition and up go the tariff barriers. Canada is similarly unrewarding because of intense U.S. competition.

The third alternative—the sterling area—presents further problems. First, many of these countries rely on primary products, the prices of which are subject to violent fluctuation, for their foreign exchange and are thus often forced to contract their imports. Second, the Russians and Chinese are sending increasing quantities of chemicals to these areas. Since in both cases they are the products of rigidly controlled economies, prices are often below ours. Mr. Chambers doubted that the glib excuse that these exports are made regardless of cost is sound. "An investigation of the facts might reveal that costs in these countries are lower than in our own and that these exports are not so uneconomic as we would like to believe." In the future both Russia and China would continue to build up their industries by ruthless control of the economy, and the writing on the wall is that they will become increasingly tough competitors.

But the total picture of British exports is not one of unrelieved gloom. Both pharmaceuticals and plastics exports are growing. Pharmaceuticals account for 15·8% of our total exports, but are only 8·8% of West German exports. The future for pharmaceuticals seems good because of the almost world-wide demand which arises rapidly for new drugs as they are discovered, and the difficulty of setting up local manufacture of such new products at the high standards needed before further progress has rendered the product or process obsolescent.

We hope that Mr. Chambers' praise for the pharmaceutical industry will be heeded by those who wish to curb its growth for the sake of fractional economies in the Health Service.

The key to new penicillins

BEECHAM Research Laboratories must feel very gratified that their first essay in fundamental research on antibiotics has come off so well. Their isolation of 6-amino-penicillanic acid—described as the basic molecule of penicillin—opens up the prospect of manufacturing literally hundreds of different penicillins by chemical, instead of microbiological, modification of the basic building brick.

Beecham decided to go into antibiotics research three years ago. Their first step was to obtain first-class advice and they were able to retain Prof. E. B. Chain, F.R.S., as their principal microbiological consultant. The successful start of their research proves the wisdom of this step. Prof. Chain has congratulated the Beecham team at Brockham Park, Surrey—Rolinson, Doyle, Naylor and Batchelor—and expresses the view that the synthesis of penicillins active against resistant staphylococcus and not producing allergic reactions in benzyl penicillin-sensitive patients would be the most important break-through in the penicillin field since the discovery of the antibiotic.

After the event it seems only common sense for Beecham to have concentrated on one proven antibiotic instead of dissipating limited resources in the search for new antibiotics by screening thousands of moulds. Perhaps it was because it was so obvious that other scientists neglected it. Having selected the target, the Beecham team attempted to produce new penicillins by chemical and microbiological means which the natural fermentation method could never produce.

It took the microbiologists the best part of a year to work out the conditions for the mould to produce one modifiable penicillin and to extract a small quantity for the chemists to work on.

In the course of the work two conventional methods of assay, microbiological and chemical, were used. Normally these methods confirm one another. Under certain conditions, however, consistent discrepancies were noted between the results of the two methods, for which there was no explanation. The chemists deduced that the brew contained an intact penicillin-like material, most probably just the core of the penicillin molecule, *i.e.* 6-amino-penicillanic acid. The proof of this deduction was to treat the brew chemically with the right reagent and produce penicillin G.

It was realised that if the material could be extracted it would be a raw material from which almost any penicillin could be made, especially those which micro-organisms could not synthesise. This has been done. So, instead of the laborious method of months of study for each new penicillin there is only one microbiological process to worry about, the remainder of the work being done in the chemical laboratory.

Chemists have never taken kindly to dependence on the dietary whims of micro-organisms for the production of antibiotics. While the Beecham

discovery does not free them entirely from this dependence, it goes a long way towards reducing the manufacture of penicillin to straightforward chemical manipulation.

Having made the discovery, how should it be exploited. Some commentators, harking back to the original discovery of penicillin and its subsequent exploitation in the U.S., argue that the same "mistake" should not be made again and that penicillanic acid should be developed exclusively in this country. Unfortunately the facts of life do not permit this. The implications of the discovery are so immense that Beecham are only likely to get reasonably rapid results by an alliance with a company already widely experienced and firmly established in antibiotics on an international scale.

Their choice has been an American company. On April 2, in New York they signed an agreement with Bristol Laboratories Inc. to collaborate in developing synthetic penicillins. Bristol have been supporting the work of Dr. J. C. Sheehan which has resulted in the total syntheses of ten penicillins (see p. 179) and have rights to exploit his discoveries. The agreement with Beecham allows them to utilise the British discoveries as well. Beecham will get royalties from the sale of new penicillins marketed by Bristol.

Additives ad infinitum

A NEW food additive law came into effect in the U.S.A. on March 5 which enforces the pre-testing of food additives by manufacturers. It is estimated that the number of food additives now in use runs into hundreds, and the preparation of a meal entirely free from them would now be extremely difficult. The march of civilisation and the growth of city populations has made these substances necessary; movement of food over long distances and extended storage means that preservatives must be added, together with mould inhibitors for foods such as bread and cheese. Emulsifiers are needed to prevent separation of the components of salad dressings; flavouring agents, stabilisers and thickeners, buffers and neutralising agents, curers, humectants, driers, colours, not to mention nutrients and enrichers, are only some of the groups of additives universally used in processed food. These substances are beneficial inasmuch as they improve palatability and prevent deterioration, provided of course that stringent safeguards are applied. The Federal Food and Drug Administration has paid tribute to the sense of responsibility shown by American industry in being ahead of the law in many respects and setting its own safety standards for food additives, with the result that no deaths and only a few cases of non-permanent poisoning have occurred in the U.S.A. during the past 20 years, in which time the list of additives has grown enormously.

The whole question now needs a radically different approach from that of 1938, when the original American Act came into force. The problem at that time was to control the use of poisonous and harmful substances and to provide safe tolerances for those which were unavoidable. Since then, knowledge of the usefulness of certain chemicals in food processing has made tremendous strides; hundreds of chemicals not used in 1938, many being then unknown, have come into use, and thousands have been considered in varying degrees. The problem of testing has got quite beyond the capabilities of the F.D.A. and has made revision of the law a necessity.

In this country the situation is paralleled, and American experience will be watched with interest, not only by those who export to that country and who have, therefore, to concern themselves directly with American legislation, but because our technological set-up is similar and the problems it raises are not unlike those in the U.S.

EXPANSION IN THE PHARMACEUTICAL INDUSTRY

We have been conducting a survey of new building projects in the British pharmaceutical industry and next month we shall publish the results of our enquiries.

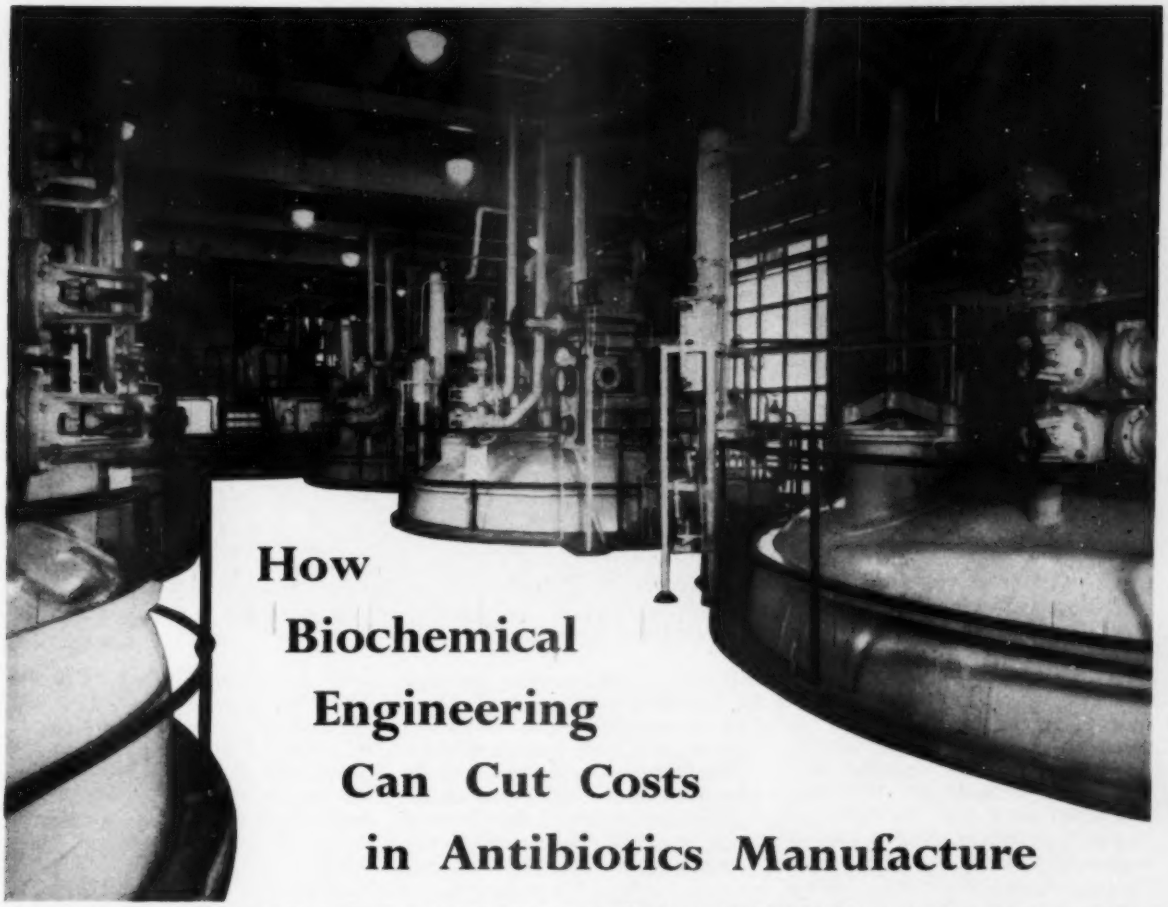
Also scheduled for publication in the May issue is a description of the new laboratories for immunological products just completed by the Wellcome Research Laboratories at Beckenham, Kent. Another highlight of the next issue will be an authoritative article on Interferon, the new anti-viral agent, by Dr. D. C. Burke, who collaborated with Dr. Isaacs on the original programme at the National Institute for Medical Research.

Untapped markets for perfume

WHY do British women spend so little on perfume? One estimate puts the *per capita* expenditure on perfume at a mere 7s. 3d. a year. At a time when women have more to spend than ever before this is a miserable sum. Is it because of some innate Puritanism? Do men object to it? Hardly, we would think, judging by the increasing expenditure on male toiletries. Is it because of the British climate which often conspicuously lacks the warmth which brings out the best in perfume? Or is it simply because the industry has muffed its publicity?

Saward Baker, the advertising agents, believe that more and better perfume publicity should be aimed at girls between 15 and 24, pointing out that this group is growing up in ignorance of the importance of perfume. Yet it has an annual spending power of £900 million a year and buys about a quarter of all cosmetics sold in this country.

Although the perfuming of cosmetics and toilet preparations is continually improving, the industry might well consider making greater efforts to exploit perfume as such. If manufacturers produce good quality perfume at a reasonable price they should be able to sell it in vast quantities. Of course purchase tax hampers sales, but on the other hand millions of women cheerfully spend more and more on highly taxed cigarettes.



How Biochemical Engineering Can Cut Costs in Antibiotics Manufacture

By J. F. Thorley, B.SC.(TECH.), A.M.I.CHEM.E.* and J. J. H. Hastings, M.B.E., M.SC., F.R.I.C.†

The antibiotics industry is extremely competitive and manufacturers are constantly striving to lower production costs. Now that the microbiologist has made his major contributions it is up to the chemical engineer to make economies by improving processing conditions and cutting plant and production costs. The biggest savings could be made by replacing batch processes with continuous fermentations. While this remains the ideal—if an extremely difficult one to achieve—smaller improvements can also contribute worthwhile economies.

IN A previous article[1] published in 1955 the first 10 years of antibiotic production were reviewed and the essential features of manufacturing techniques were discussed.

It is appropriate at this stage to consider the lines along which advances continue to be made or examined.

The microbiologist has already supplied his major contributions to practice, although there is no doubt that fundamental studies on metabolism and cell reproduction will continue with most of the major antibiotic - producing organisms. These are unlikely to give rise to major changes in equipment or method, although they may well affect nutritional requirements and details of fermentation control. On the other hand, new antibiotics may well be discovered which will not be amenable to the now traditional methods of extraction and recovery, and will require a new path to reach the finished product. It may well be that the use of solvent transfer, adsorption by ion-exchange resins, or the precipitation of insoluble intermediates, will be replaced, for example, by electrophoretic or chromatographic separation on a scale not hitherto contemplated.

All stages of antibiotic manufacture still provide a happy hunting ground for the chemical engineer. This has been recognised by the universities, which have now made provision for chemical engineers interested in biochemical processes.

* Development Chemical Engineer, and †Technical Director, Distillers Co. (Biochemicals) Ltd.

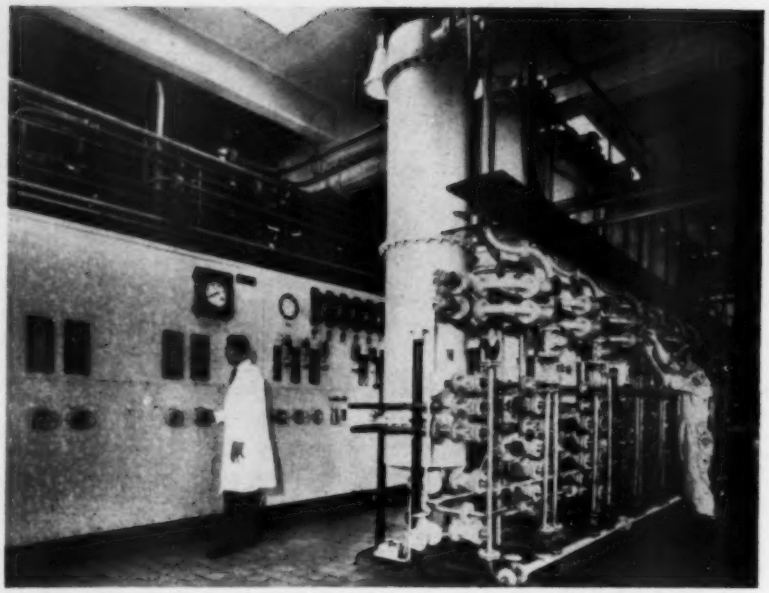
Above: Mechanically agitated 20,000 gal. fermenters for antibiotic production.

The biochemical engineer or chemical engineer employed in industries which utilise the methods of biochemists for production processes requires a wide field of knowledge and an extensive vocabulary. In many of the other process industries it is sufficient for the chemical engineer to know the language of his own art and to have some acquaintance with the terminology of the chemist and the mechanical engineer. This is not so in present-day biochemical factories, and the biochemical engineer must be acquainted with the ideas of the microbiologists, pharmacists and pharmacologists, as this field of operation is one in which many scientists combine to form an integrated whole.

Biochemical engineering

The duties of the biochemical engineer cover a wide field in an expanding industry. It is essential that plant design and development should keep abreast of developments in the use of various materials of construction, particularly the lesser known materials such as plastics. Although development work has taken place in the industry, often new methods are developed for other uses and the chemical engineer should be quick to adapt such equipment for his own purpose. Developments in pumps, valves, glands or shafts have in recent years had a considerable effect upon the ease with which some large-scale biochemical processes can be carried out. Many of these new techniques owe their origin to the even newer field of nuclear engineering, a science which again makes highly critical demands upon existing equipment. To some extent these two branches of chemical engineering have similar requirements in that it is essential that no contamination should occur at any point of the process equipment.

In the case of the nuclear engineer, one of his major problems must be to prevent the escape from closed systems of "contamination" in the form of radioactivity. The biochemical engineer of today has the task of preventing the entry to closed systems of " contamination," in the form of infecting micro-organisms. He must, however, be prepared to look forward to the time when valuable products may be made from deadly organisms in pure culture, when his problem will become in many respects identical with that of the nuclear engineer. In view of the vast sums of money that are now being spent on nuclear research, it is likely that many of the outstanding problems will first be solved in the latter field, and the biochemical engineer should make it his duty to become acquainted with these advances wherever he can.

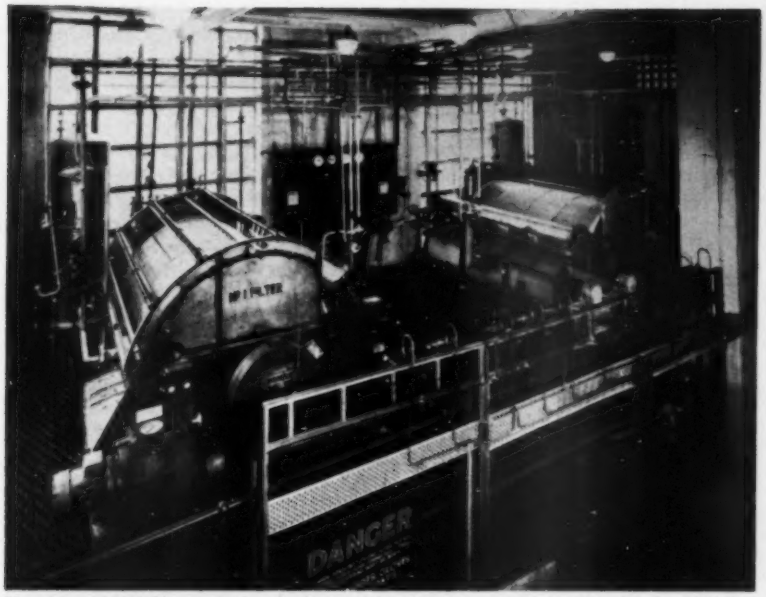


Ion exchange columns and control panel for extraction of streptomycin from fermented broth.

Economic problems

In the antibiotics field, which is only a part of the complete range of biochemical activities, a wide range of drugs is now available for treatment of a variety of diseases and conditions. These may broadly be divided into two groups, the broad spectrum antibiotics such as the tetracyclines and the narrow spectrum antibiotics such as penicillin and streptomycin. It is true to say that no drugs have been developed recently which have achieved the world-wide acclaim which was given to penicillin, and in view of the range of illnesses which can be treated by the existing drugs there is less chance of similar epoch-making discoveries taking place. There is no doubt that the antibiotic industry is one in which there is intense competition. During recent years the price of most antibiotic materials has fallen substantially, in spite of major increases in the cost of labour and materials during the same period.

Other branches of the biochemical industry have similar economic problems. Competition from petroleum chemicals has already seriously affected the production of alcohols by fermentation and the two fields which are likely to remain the largely undisputed territory of the biochemical industry are the manufacture of potable spirits and antibiotics. In this latter industry it is clearly the duty of the chemical engineers to ensure that the processes and equipment used are such that they yield a maximum amount of saleable products in the most economical manner. The capital investment required for the provision of a new antibiotics programme is higher than that required for a similar venture in many other branches of the chemical industry. With the increasing use of stainless steel, the cost of process equipment is extremely high. Large quantities of raw materials are required for fermentation and as many of these, such as molasses and soya meal, are imported larger stocks are often held than would be required for home-produced raw materials, and a high capital investment is required for this purpose. Other operating costs, beside the inevitable maintenance, are the provision of large quantities of steam for sterilisation of vessels and mashes, compressed air for aeration in aerobic fermentation, electrical energy for agitation and cooling water to remove the heat produced both by the fermentation process and by the transfer



Vacuum precoat filters continue to be used for the removal of mycelium from antibiotic fermentations.

of mechanical energy from the agitators into the medium.

Most industrial fermentations are carried out at present as a batch process, and if a look be taken at other industries such as petroleum it will be seen that in the interest of economy and ease of production, batch-wise methods are steadily being replaced by continuous automatically controlled processes, the optimum production programmes being determined by the use of computers and linear programming. It will be some time before the biochemical industry has caught up with such techniques, but there are obvious advantages to be gained by the intelligent application of these methods. The chemical engineer should aim at devising means by which the capital cost of equipment can be reduced, the service requirements smoothed out and the plant utilisation increased in order to reduce the overall manufacturing cost. Looking into the future of any such complicated science is difficult and may be considered to be a hazardous occupation. In a short while new methods or processes may be developed which may change the entire position overnight. Such changes are likely to be change of emphasis rather than of general principle. It appears useful to survey the present position of two of the main problems, agitation/aeration and continuous fermentation, and to visualise the lines along which development is likely to occur in the future.

Air sterilisation

In the previous review in this journal[8] an outline was given of the methods used for sterilising the air in antibiotic fermentation. Since this review was given there has been little progress in this field and scrubbing by carbon or slag wool beds is still accepted as the current procedure. Recently, however, so-called absolute paper filters have been developed by various manufacturers. These are claimed to be 99·95% efficient as measured by the Methylene Blue Test B.S.S. 2831/1957. Although this order of efficiency is probably sufficient for the supply of air into certain sterile atmospheres, it is not generally considered to be good enough for a fermentation where large volumes of air are blown into the fermenter for say 200 hr. This type of filter has the advantage that the pressure drop is only of the order of 1 in. w.g., and 250 c.f.m. per sq. ft. of filter area can be obtained as a normal flow rate. A further development of this type of filter may provide a method suitable for fermentation, and if this can be done the outlet pressure of the air compression system will be considerably reduced, with substantial saving in power requirements. Elsworth *et al.*[2] have developed a method of sterilising air by heat in a unit having a capacity of 1,700 litres per min. Using this equipment it was shown that the survival rate of spores was less than 1 in 5 million. Although economically it is unlikely that such methods can be used generally on a large scale, there may be special fermentations with minimal air demands where the additional insurance is well worth while. The technique is of continuing interest and shows the high degree of sterility which is regarded as desirable in pure culture antibiotic fermentations.

Oxygen

Nearly all the important industrial fermentations follow a common technique. The sterile nutrient solution is placed in a deep vessel of up to 20,000 gal. capacity and inoculated with the micro-organisms. This mash is then aerated by forcing air into the base of the vessel through some form of sparger, and often mechanical agitation is provided to improve the distribution of the air throughout the suspension. For the fermentation to proceed it is essential that the micro-organism is supplied constantly with oxygen.

Theoretically this may reach the organism in two ways. Firstly by a series of diffusion stages in which the oxygen dissolves into the water and diffuses through the cell walls, and secondly by direct contact between the air bubbles and the cell walls. It is generally accepted that most of the oxygen reaches the cells by the diffusion process, and in fact Chain *et al.*[3] have demonstrated that only dissolved oxygen can be utilised by selected micro-organisms. There is some evidence by Bartholomew *et al.*[4] that oxygen transfer can occur when the cells are in momentary contact with the gas-filled interface. Oxygen is only slightly soluble in water and for this reason forms only a small reservoir in solution. This reservoir is depleted by a respiring organism and it is necessary to replace consumed oxygen by some efficient and continuous process. It is usually accepted that the absorption of oxygen by micro-organisms in a nutrient solution is a special case of absorption with the liquid film controlling the rate. It is thought that the cell wall offers negligible resistance, and in support of this theory it has been shown that above a certain critical oxygen concentration the uptake of oxygen by micro-organisms is independent of

the oxygen concentration in the liquid. This has been reported by Finn,[5] who summarised his evidence mainly with respect to single cells. In a submerged mould fermentation there is a likelihood that large clumps of mycelium may occur and these may cause some resistance to the diffusion of oxygen. Little information is available on the degree of agitation required to disperse these clumps, but it is usually held that the agitation required to maintain maximum rate of oxygen solution will also prevent clumps from forming.

Several methods have been developed for a determination of the overall mass transfer coefficient. The sulphite method developed by Cooper *et al.*[6] measures rate of diffusion of oxygen into water, but can only be applied to fermentation processes with caution because of the differences in the physical system. It does, however, offer a convenient method of comparing the aeration efficiency of different fermentation equipment. An alternative method is the use of the polarograph. This has been developed by Chain *et al.*,[3] but again there are disadvantages in practice. Further developments by Bartholomew *et al.*,[4] and Berman *et al.*[7] have suggested methods to overcome some of these difficulties. Although this theory is conveniently simple, it is thought by many workers that the diffusion of oxygen into the culture is not so straightforward, and considerable work is still necessary before a complete theory can be proposed.

To ensure that oxygen is thoroughly distributed in the system, mechanical agitation is usually applied in deep fermentations. This agitation disperses the air into small bubbles, thus increasing the interfacial area. Secondly the agitation lengthens the bubble paths and hence the contact time in the liquid, and thirdly the clumps of mycelium are broken down. In general fermentation processes it has become standard practice to use an air sparger situated at the bottom of the vessel with an agitator a short distance above it. The dimensions of such a vessel are shown in Fig. 1. There are many types of sparger in common use, a rather novel type being a diaphragm sparger in which a pierced rubber diaphragm is held around its head to a perforated backing plate, the pressure of the air through the

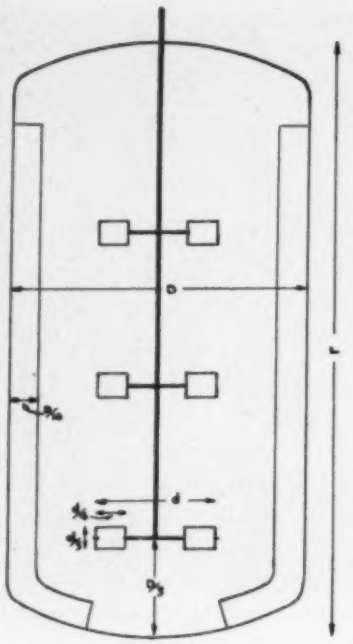


Fig. 1

backing plate causing the diaphragm to expand so that the air emerges in many streams of small bubbles. This type of sparger has the advantage of a sintered glass sparger, while the elasticity of the diaphragm prevents blockage due to mycelial growth. The most common type of sparger may even consist of a single open end or alternatively a ring or branched pipe with holes drilled in its surface. In practice it is found that whilst the design of the sparger is important with small vessels, there is considerable latitude of design for satisfactory aeration in large industrial fermenters.

The turbo mixer type of agitator as shown in Fig. 1 is probably the commonest in use today, other types being an inclined blade with plates at 45°, or paddle type agitators where only mild agitation is required. With the turbo mixer it is usual for the fermenter to be designed for fully baffled conditions as shown in Fig. 1. Because of the high cost of compressed air and mechanical agitation, it is important to make the best possible use of these two services.

The power released by the air contributes very substantially to the agitation of the medium, but power input via the agitator can usually be demonstrated to be the more economic approach. The degree of agitation is usually quoted in terms of horse-power input, and this may well be a reliable method, providing that design gives a good distribution of turbulent motion within the vessel. The correlation of power input and mixing efficiency is, however, open to doubt and it is not considered that this is the entire story.

It is possible to obtain much the same results from the fermentation with several combinations of aeration and mechanical agitation. As the costs of these services are different the choice of a combination for any particular fermentation is obviously determined by economics. Studies have shown that for penicillin fermentations there is a minimum air rate for any given shaft power input below which the yield falls away sharply. If the agitator output is increased then the minimum air rate decreases to a new limit. These conditions, when applied to a particular fermentation, usually indicate that the total cost of aeration and agitation passes through a minimum value which is then related to the yield in the fermenter, and allows the optimum conditions to be selected.

CONTINUOUS FERMENTATION PROCESSING

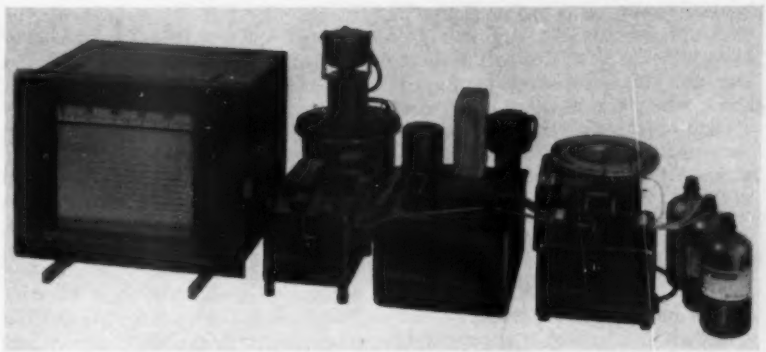
At present most fermentation processes are still carried out as batch operations. A continuous process where the material containing the necessary growth substance is fed continuously into the vessel and the desired products continuously withdrawn at the same rate, has many potential advantages, the first of which is reduction in non-operational time. The output of a fermenter can be increased in direct proportion to the change in plant utilisation, and the operations of emptying, cleaning, sterilising and recharging a batch fermenter are all a dead loss for the manufacturer.

A second factor is that greater uniformity of product should result from continuous operation, with the further advantage that higher efficiency of product recovery is likely to be achieved with a constant feed, particularly if this recovery can also be carried out on a continuous basis.

A further advantage of continuous processing is the steady rate of demand on services, which means that the boiler house and air compression equipment can be smaller per unit of fermenter capacity, and that no extra charges are incurred by high peak electrical load conditions.

Continuous processing has already been successfully applied to the yeast fermentation industry and to certain types of industrial alcohol fermentations. There are certain disadvantages which have restricted the use of such processing in the manufacture of antibiotics. These include the serious dislocation caused by a breakdown of the fermentation, the high standard of plant construction and control necessary to ensure that such a breakdown does not occur, but chiefly the complexity of the biochemical processes involved. At the moment a knowledge of these processes has not advanced to the stage where it can be shown that a continuous process will necessarily provide a higher output of desired product. The use of continuous processing depends entirely upon the economic advantages to be gained, and these are likely to be greatest where a large volume of production is required. Several antibiotic fermentations, although technically significant, would not benefit greatly from continuous control, as the quantity of product required for sale is small in terms of weight and not likely to increase appreciably in the future. Although some improvement may be possible in the production of these materials by continuous methods, obviously it is a greater economy that efforts should be directed at materials like penicillin where the present-day volume of production is large enough to justify the development work required.

Continuous fermentations may be carried out in one or a series of vessels with or without recycling part of the product. The control of the unit may be based on one of two methods. In the first the throughput rate is maintained at a constant value. The concentration of cells and other products is then dependent upon this throughput rate and other variables such as the nutrient concentration. In the second method the cell concentration is maintained at a constant level to give a predetermined value of output. In practice the second system is more difficult to establish and is mainly employed as a research tool.



Modules comprising the standard Technicon autoanalyser system for laboratory analysis of individual samples. The equipment is capable of analysing 40 or 60 samples per hour.

As an interim measure, semi-continuous operation may have some advantages. In this method a fraction of the fermenter contents is removed at regular intervals and replaced by an equal volume of new culture medium. These aspects of continuous fermentation have been covered by Ricica[9] and more generally at a symposium held in Prague in June 1958,[10] of which the Ricica paper formed a part.

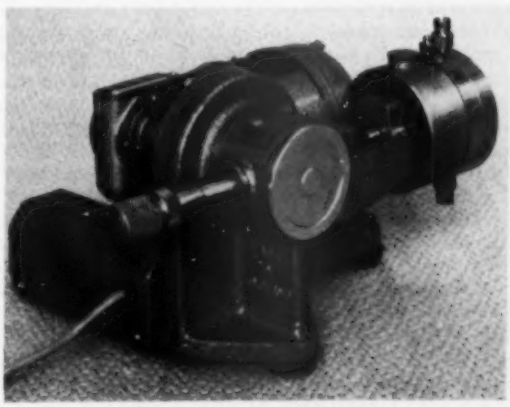
Theoretical background

There have been several attempts to formulate a suitable theoretical background for continuous fermentation. The simplest case for such treatment is where the growth rate is controlled by the concentration of a single limiting nutrient. Monod[11] and Novick and Szilard[12] developed basic theories for these conditions.

Golle[13] developed a theoretical method for the system in which the growth rate is assumed to be independent of the concentration, and Maxon[14] later reviewed these papers and extended them to cover multi-vessel systems, recycling, and fermentations in which intermediate metabolites are required. Herbert *et al.*[15] also developed this approach, using it to calculate the increased output which can be obtained from a continuous operation. Such theories, which are the only ones to have been thoroughly developed, are applicable to fermentations such as the growth of bacteria or yeast in a homogenised mash, the growth rate being dependent upon the concentration of a single nutrient.

In 1950 Monod[11] derived a relationship to define the steady state conditions which exist in a continuous fermenter and the rate of turnover which can be achieved with such a system. The important characteristics of a fermenter are the output rate of cells per unit of fermenter capacity and the efficiency of utilisation of the nutrient medium. With regard to cell output, Herbert[15] has given comparisons of continuous and batch production and has found that for typical values of the variables involved, a continuous fermenter can have a cell output between 4 and 12 times the output of a batch fermenter of comparable size.

Theoretical study of the efficiency of utilisation of a limiting substrate in continuous fermentation compared with an equivalent batch process has shown that the ratio is always less than unity, but for



Metering pump with micrometer adjustment and diaphragm head, for continuous addition of sterile nutrients or reagents to fermentations.

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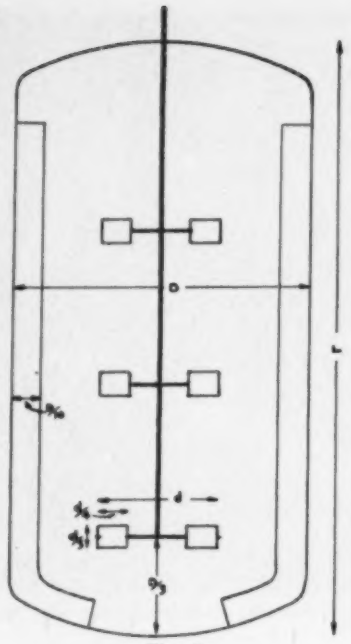

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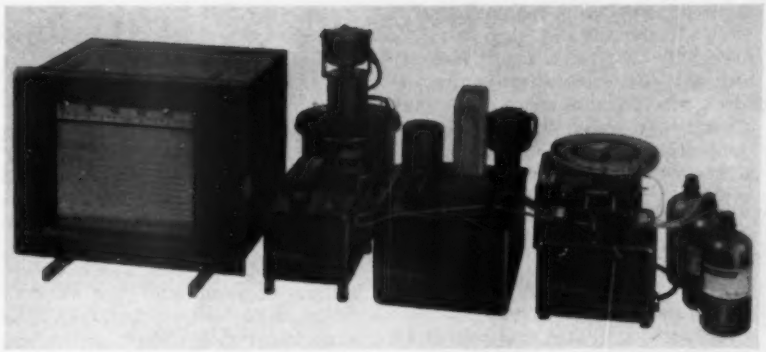
Continuous processing has already been successfully applied to the yeast fermentation industry and to certain types of industrial alcohol fermentations. There are certain disadvantages which have restricted the use of such processing in the manufacture of antibiotics. These include the serious dislocation caused by a breakdown of the fermentation, the high standard of plant construction and control necessary to ensure that such a breakdown does not occur, but chiefly the complexity of the biochemical processes involved. At the moment a knowledge of these processes has not advanced to the stage where it can be shown that a continuous process will necessarily provide a higher output of desired product. The use of continuous processing depends entirely upon the economic advantages to be gained, and these are likely to be greatest where a large volume of production is required. Several antibiotic fermentations, although technically significant, would not benefit greatly from continuous control, as the quantity of product required for sale is small in terms of weight and not likely to increase appreciably in the future. Although some improvement may be possible in the production of these materials by continuous methods, obviously it is a greater economy that efforts should be directed at materials like penicillin where the present-day volume of production is large enough to justify the development work required.

Continuous fermentations may be carried out in one or a series of vessels with or without recycling part of the product. The control of the unit may be based on one of two methods. In the first the throughput rate is maintained at a constant value. The concentration of cells and other products is then dependent upon this throughput rate and other variables such as the nutrient concentration. In the second method the cell concentration is maintained at a constant level to give a predetermined value of output. In practice the second system is more difficult to establish and is mainly employed as a research tool.



Modules comprising the standard Technicon autoanalyser system for laboratory analysis of individual samples. The equipment is capable of analysing 40 or 60 samples per hour.

As an interim measure, semi-continuous operation may have some advantages. In this method a fraction of the fermenter contents is removed at regular intervals and replaced by an equal volume of new culture medium. These aspects of continuous fermentation have been covered by Ricica[9] and more generally at a symposium held in Prague in June 1958,[10] of which the Ricica paper formed a part.

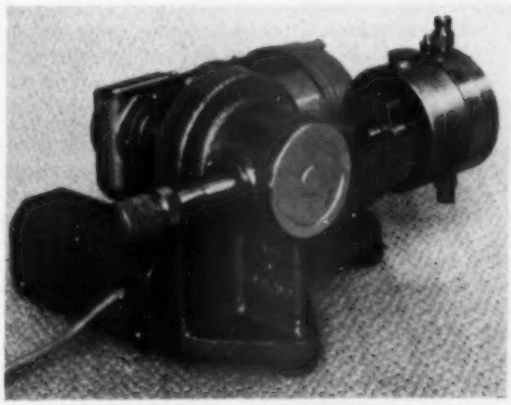
Theoretical background

There have been several attempts to formulate a suitable theoretical background for continuous fermentation. The simplest case for such treatment is where the growth rate is controlled by the concentration of a single limiting nutrient. Monod[11] and Novick and Szilard[12] developed basic theories for these conditions.

Golle[13] developed a theoretical method for the system in which the growth rate is assumed to be independent of the concentration, and Maxon[14] later reviewed these papers and extended them to cover multi-vessel systems, recycling, and fermentations in which intermediate metabolites are required. Herbert *et al.*[15] also developed this approach, using it to calculate the increased output which can be obtained from a continuous operation. Such theories, which are the only ones to have been thoroughly developed, are applicable to fermentations such as the growth of bacteria or yeast in a homogenised mash, the growth rate being dependent upon the concentration of a single nutrient.

In 1950 Monod[11] derived a relationship to define the steady state conditions which exist in a continuous fermenter and the rate of turnover which can be achieved with such a system. The important characteristics of a fermenter are the output rate of cells per unit of fermenter capacity and the efficiency of utilisation of the nutrient medium. With regard to cell output, Herbert[15] has given comparisons of continuous and batch production and has found that for typical values of the variables involved, a continuous fermenter can have a cell output between 4 and 12 times the output of a batch fermenter of comparable size.

Theoretical study of the efficiency of utilisation of a limiting substrate in continuous fermentation compared with an equivalent batch process has shown that the ratio is always less than unity, but for



Metering pump with micrometer adjustment and diaphragm head, for continuous addition of sterile nutrients or reagents to fermentations.

typical examples it is found that a value of over 0·9 is common. A lower efficiency of this order therefore only becomes of major importance where the nutrient cost forms a very high proportion of the total manufacturing cost, as for example some intermediate biological conversions of steroids.

Unfortunately many biochemical processes are not as simple as those taken as the basis of such an analysis. Some of the relationships which have been regarded as constant are not in fact true constants, the metabolic behaviour of the organisms being dependent upon such things as the dilution rates or the growth rates in the system. Toxic metabolic products may become over-controlling factors, for example, the inhibiting effect of alcohol concentration in yeast fermentations. Insufficient oxygen concentration may limit growth in aerobic fermentations and under such conditions several metabolic processes may occur simultaneously. A further complicating factor is the fact that many of the raw materials used as nutrients for fermentations are complex mixtures of different carbon and nitrogen compounds, varying in their suitability as metabolites. These more complicated fermentation conditions probably require multi-vessel continuous fermentation plant, so that residence time, dilution rate and nutrient concentration in each section are the optimum to enable the different metabolic processes to proceed as desired and the various materials present in the nutrient to be used to the best advantage.

Work in this field has been reported by Alshalter *et al.*[16] and Ruff *et al.*[17] and Ericsson.[18]

Brown[19] has shown that, using *Streptomyces griseus*, the yield of streptomycin from a single-stage continuous process can approach that of a batch culture. Other workers have been less successful and have found considerable evidence of mutation of the organism to non-streptomycin producing strains.

For some years this problem of mutation received considerable prominence, but in spite of the example quoted it is now not considered to be so outstandingly important as was originally expected. A new mutant will only become a large fraction of the total cell concentration if it can grow more rapidly in the medium than the original organisms, and in this case the mutant will eventually completely replace the original strain. Unless the mutant lacks some desired quality or has a lower power to produce the fermentation product, this may in fact be a valuable change, as the dilution rate and hence fermenter output can be adjusted to suit the new organism. Obviously the system that can use a high dilution rate has the best chance of remaining free of contamination or mutation. The situation is more complicated where the nutrient contains several feed sources, as it is possible that a mutant may be able to metabolise fractions of the substrate not available to the original organism.

It will be plain even from this brief treatment of the dynamics of this type of process that control of many variables is essential in order to attain the optimum conditions and therefore give the most economic product. Whereas manual control gives tolerably good results in a batch fermentation, it is unlikely that this could be the case with continuous processes. It is clearly necessary to monitor continuously such variables as *pH*, temperature, feed concentration and dilution rate, as these variables will considerably alter the yield obtained from fermentation. Another important consideration is that of foam control. It is well known that under some conditions fermentation tends to form a stable foam which is a serious embarrassment. In any continuous plans it may be necessary to employ a system which will detect foaming and immediately add a quantity of anti-foam agent. Such a system has been described on pilot scale by Bartholomew[20] and is in some cases employed in full-scale batch fermentations.

pH control problems

*p*H control still presents some problems. Until recently it has not been possible to obtain electrodes which will stand sterilisation temperatures and give reliable results. It is also important that the cells and debris present in the fermented mash do not cause trouble at the salt bridge of the electrode. The location of the *p*H electrode assembly is of the utmost importance. A location in an external pipe system has some advantages in that it is possible to sterilise the equipment by chemical means, and also in the event of electrode failure it is a simple matter to shut off this side stream and to replace the broken electrode. It is uncertain, however, whether chemical sterilisation can always be accepted on the larger scale, and this system introduces some difficulties in control when the *p*H is changing rapidly, due to the delay which is introduced by the system lag. It would be preferable to have electrodes which are immersed in the body of the fermenter, but again there are many engineering problems to be solved before a reliable system is evolved. Physical variables such as temperature and air flow are easily controllable by methods well established in the chemical and engineering industry.

The problem of controlling nutrient concentration continuously can present some difficulties, but there are several methods available which offer possibilities of development although the design of suitable instruments may be one of the difficult features of this problem. It may be possible to use specific gravity, optical rotation or infra-red spectroscopic analysis. Recently a very practicable technical instrument for auto-analysis has been developed in the United States, and several of these units are already in industrial use in this country. Successive liquid samples are fed through the unit at a very high rate, being separated by controlled air or gas bubbles. End-points are determined colorimetrically or by other physico-chemical methods, and it is therefore possible to follow quite closely any rapid changes in the process under observation.

It is a strong point in favour of continuous fermentation that the process is largely self-balancing when a steady state has been established. Nevertheless, it is an advantage to have rapid and accurate control instruments in arriving at the desired steady state, and for detecting any unexpected deviation from normal behaviour.

It can be seen from this discussion that before embarking on extensive research on any particular continuous fermentation, a careful assessment of the possible economic advantage should be made. In some cases it can already be seen that even if the maximum possible advantage is achieved in changing from batch to continuous fermentation, the improvement is still not enough to defend fermentation from competing synthetic processes.

(Concluded on page 155)

Pharmaceutical Dispersions of Solids in Liquids

A GUIDE TO THEIR FORMULATION

By David Jack,* B.SC., F.P.S., A.R.I.C.

The author sets out some of the principles which have been found in practice to be important in formulating pharmaceutical suspensions. Theoretical arguments have been kept to a minimum in an endeavour to provide a simple and reliable guide to the formulation of suspensions of solids in liquids.

MANY pharmaceutical preparations consist of suspensions of solids in liquids. Nevertheless, the principles governing the formulation of such suspensions have received very little attention in pharmaceutical literature. Most pharmacists are familiar with preparations which sediment on standing and in which the solid is difficult to redisperse by shaking. This situation is usually met by decreasing the particle size of the dispersed solid and by making the vehicle more viscous. While these measures always delay sedimentation, in time the end-result is usually worse than before, since, after sedimentation, the solid is even more difficult to redisperse by shaking. In extemporaneous dispensing this is seldom serious, but commercial products of this kind would be virtually unsaleable.

Accordingly, it was felt desirable to record some of the principles which have been found in practice to be important in formulating pharmaceutical suspensions. In this discussion, theoretical arguments have been kept to the minimum required to rationalise the subject in order to avoid losing practical aspects in too much detail. As a result, it may be that oversimplifications have been made, but it is believed that the arguments given provide a simple and reliable guide to the formulation of suspensions of solids in liquids. Detailed treatment of solid/liquid systems may be found in reference works.[1, 2]

Wetting

Many solids such as procaine penicillin, most sulphonamides, steroids, etc., do not wet spontaneously when shaken with water. Usually, if the solid is finely divided, it separates to the surface as a substantially unwetted mass frequently entrapping air to form a solid-stabilised foam. Since wetting is replacement of solid-air interfaces by solid-liquid interfaces, for a solid to wet spontaneously in a liquid it is necessary for the solid-liquid interfacial energy to be less than the solid-air interfacial energy, *i.e.* $E_{S.A.} > E_{S.L.}$. Conversely, if $E_{S.A.} < E_{S.L.}$, the solid will not wet spontaneously in the liquid. When a water-soluble wetting agent is added to a mixture of one of the above solids and water, $E_{S.L.}$ is reduced and wetting occurs.

Deflocculated systems

When excess water-soluble surface active agent is added to a mixture of a poorly-wetted, finely-divided solid and water, wetting occurs and the solid is dispersed as single particles in the liquid. This may be checked by microscopic examination of the suspension. When such a suspension is allowed to stand, sedimentation occurs slowly, but the particles pack very closely to form a sludge which is difficult to redisperse by shaking.

This generalisation may be checked by adding about 0·5% of *Tween* 80 to a 10% w/v suspention of sulphadimidine in water. Without the wetting agent, most of the solid separates to the surface of the mixture even after shaking. After adding the wetting agent, a close-packed sediment is formed when the suspension is allowed to stand.

A system in which the particles are dispersed as individuals is said to be deflocculated and the close-packing on sedimentation is called "claying." The latter name is derived from the fact that clay was formed by sedimentation of a deflocculated suspension. Provided the particles are not colloidal, deflocculated systems exhibit the following general characteristics.

1. Slow sedimentation, usually with formation of a cloudy supernatant fluid due to the presence of fine, deflocculated particles.
2. When sedimentation is complete, the sedimentation bulk is small and the sediment is difficult to redisperse.
3. The viscosity is substantially Newtonian, provided the concentration of solids is not too high (less than about 30% w/v.)

Flocculated systems

Consider a hypothetical solid-liquid system in which $E_{S.A.} > E_{S.L.}$ but in which $E_{S.L.}$ is still significantly high. The solid wets but the system arranges itself to a minimum free energy state. Clearly, for a given system, the total free energy may be reduced by reducing the solid-liquid interfactial area. This is accomplished by the solid particles adhering to each other to form agglomerates, thereby replacing some part of the solid-liquid interface with solid-solid interface.

Because of the agglomeration, the average particle size of the system is large compared to the individual particles so that sedimentation occurs rapidly. However, the agglomerates pack loosely so that the sedimentation bulk is large and redispersion is easy. A system of this type is said to be flocculated, the agglomerates of particles being called floccules.

Flocculated systems exhibit the following general properties.

1. Rapid sedimentation with formation of a clear supernatant fluid.
2. When sedimentation is complete, the sedimentation bulk is great. redispersion is easy.
3. Non-Newtonian viscosity, the apparent viscosity being greater with increasing flocculation.

* Head of Laboratory Services, Smith Kline and French Laboratories Ltd.

Flocculated systems may be demonstrated by repeating the experiment described previously for an aqueous suspension of sulphadimidine varying the concentration of *Tween* 80 from 0·0 to about 0·1% when, with increasing concentration of *Tween*, a progressive deflocculation will be observed giving decreasing sedimentation bulks and increasing difficulty of redispersion.

Generalisations

1. If $E_{S.A.} < E_{S.L.}$, the solid does not wet spontaneously.
2. If $E_{S.A.} > E_{S.L.} \fallingdotseq 0$, the solid wets and is deflocculated.
3. If $E_{S.A.} > E_{S.L.} > 0$, the solid wets and is flocculated.

Further considerations of deflocculation and flocculation

In considering flocculated and deflocculated systems, the difference in behaviour has been explained on the basis of differences in interfacial energies. Although this simple concept is helpful in rationalising the behaviour of these systems in an easy way, a further consideration is the presence of an energy barrier at the solid surface which prevents adhesion of the particles. The barriers consists of two factors. Firstly, surface electrical charges resulting from adsorption of surface active agent or ions at the surface and which prevent adhesion of particles by electrostatic repulsion. Secondly, the solid surface becomes solvated, the solvated sheath keeping the particles apart mechanically. Flocculating agents may act by decreasing the surface charges or the degree of solvation, or both, thus allowing adhesion of the particles. The adhesive forces prevent close-packing on sedimentation by the floccules adhering and thus forming a loose sediment of some mechanical rigidity so that further sedimentation does not occur. The adhesive forces are also the source of the increased viscosity.

Practical formulation of suspensions

The following characteristics are required in a satisfactory pharmaceutical suspension.

1. The sediment must be easily dispersed by shaking. A large sedimentation bulk is usually desired.
2. The dispersed solid must remain suspended long enough for an accurate dose to be withdrawn.
3. The suspension must flow readily.

Treatment of solids which are poorly wetted or highly flocculated

With solids which are naturally poorly wetted or highly flocculated in the selected vehicle, it is usually easy to obtain the above characteristics. Easy dispersion is assured by controlling the input of wetting agent and the particle size (surface area) of the solid to obtain a controlled degree of flocculation in the finished suspension. In general, fine particles and low concentration of wetting agent give a large sedimentation bulk. One must beware of producing too great flocculation because of the danger of formation of thixotropic or pseudoplastic-systems. Even if the preparation flows readily, air is often entrapped when a highly flocculated suspension is shaken and the product becomes unsightly.

Adequate suspension of the solid is obtained by adjusting the viscosity of the vehicle. In aqueous systems this is usually done by addition of hydrophilic colloids such as sodium carboxymethyl-cellulose, methyl-cellulose, sodium alginate, acacia, tragacanth, etc. Since most substances of this type have some surface active properties, it is advisable to titrate the solid with wetting agent in presence of the selected suspending agent because subsequent addition of suspending agent may alter the degree of flocculation in the finished preparation.

Aqueous suspensions of procaine penicillin or other sparingly-soluble penicillin salts, and of cortisone or other steroid hormones, are typical examples of products formulated on the above principles.

In formulating products of this type for injection, it is essential that the solid be completely wetted. Unwetted fine particles may build up on the tip of the hypodermic needle when the suspension is being drawn into the syringe or jam in the needle when injection is attempted. Lubrication of hypodermic syringes with silicone fluids or other oils may also introduce a complication with suspensions of low-surface-energy solids. It has been explained that in order to obtain an acceptable pharmaceutical suspension a certain degree of flocculation is essential and that this in turn results from a system in which $E_{S.L.} > 0$. When such a suspension is placed in a silicone-lubricated syringe, the solid may be preferentially wetted by the silicone (since silicones have low surface energy and $E_{S.Silicone} \fallingdotseq 0$) and stick to the side of the syringe. When injection is attempted the plunger "freezes" in the barrel. This problem may be overcome either by adding more wetting agent to the suspension so the $E_{S.L.} = 0$, but clearly this would produce a suspension which could not be stored without "claying"; or more satisfactorily, by not using lubricated syringes. An emulsion of a solid/oil dispersion in water might also be satisfactory, but to the author's knowledge this has not been tried.

Suspensions of this type are usually packed in silicone-treated vials if the active ingredient is at all expensive, to ensure that nearly all of the product may be withdrawn. In order to obtain rapid drainage of suspension from the silicone surface, the surface energy of the suspension should be as high as possible, but for clean drainage complete wetting is necessary. The apparent anomaly between these conditions and the behaviour of such a suspension in lubricated syringes may be explained by the fact that silicones used for treating vials form solid films when "cured" by heating, whereas silicones used for lubricating syringes are selected because of their heat stability and so remain fluid even after sterilisation by heat.

Calamine Lotion B.P. 1948 is an example of a highly flocculated system which, because of the high specific gravity of the solid ingredients, sediments vary rapidly. In the B.P.1953 bentonite was added to give the vehicle some rigidity, so that the calamine and zinc oxide are supported mechanically but the end-product is often thixotropic. In the B.P.1958, the system is made fluid by addition of sodium citrate which causes some deflocculation.[3] Electrolytes such as sodium citrate or sodium hexametaphosphate may bring about deflocculation by adsorption of the anion resulting in increased surface change and probably increased hydration of the solid surface. Deflocculation of the calamine and zinc oxide could also have been achieved with a water-soluble wetting agent.[4, 5]

In oils, polar solids usually produce flocculated suspensions which may be deflocculated and rendered fluid with oil-soluble wetting agents. For example, in chocolate manufacture dried milk protein is deflocculated by addition of lecithin.

Solids which are naturally deflocculated

Solids which are naturally deflocculated and "clay" in the selected vehicle may be treated in two ways.

1. The solid particles may be flocculated by suitable additives.
2. The vehicle may be given a degree of rigidity sufficient to support the particles mechanically.

Flocculating agents have the effect of increasing $E_{s.L.}$ or reducing the charge and/or the degree of solvation of the solid surface. For example, deflocculated aqueous suspensions may be flocculated by addition of a small amount of cetrimide or other quaternary wetting agent because the first layer of wetting agent forming on the particles is oriented carbon chain outwards.[1] This first layer is very firmly bonded to the solid surface and is not readily removed by washing. Further addition of cationic produces progressive degree of deflocculation since a second layer of cationic is adsorbed polar end outwards. By controlling the particle size of the solid and the input of cationic agent, it is possible to produce a suspension with the desired degree of flocculation. In general, if an amphipathic surface active agent is adsorbed at a solid-liquid interface with its non-polar end oriented towards a polar solvent, or with its polar end towards a non-polar solvent, flocculation is possible. For example, procaine penicillin is deflocculated and "clays" in arachis oil, but addition of a small amount of *Tween* 80 gives a "non-claying" flocculated suspension because the *Tween* is absorbed with the polyoxyethylene chain oriented towards the oil.[6]

Use of gelling agents

The use of bentonite in calamine lotion to produce a vehicle with some degree of mechanical rigidity has already been mentioned. In general, if the thixotropic force or yield point of the vehicle is greater than the weight of the particles, suspension of a deflocculated solid is possible. For example, procaine penicillin may be suspended in arachis oil or mineral oil gelled with aluminium stearate. In the case of the arachis oil gel, some flocculation of the particles may also occur due to formation of amphipathic molecules by oxidation of the oil if it is exposed to air whilst the gel is being made. In these systems, the aluminium stearate forms a molecular lattice-work which gives the gel a certain rigidity at rest. Introduction of a small amount of a polar substance such as glycerol disrupts the lattice-work, the system becomes fluid and the procaine penicillin "clays."

Foaming in suspensions of solids

Foaming in suspensions of solids usually results either from the presence of unwetted fine particles or the low surface tension of the system.

In the case of solid-stabilised foams, it is necessary to increase the concentration of wetting agent to ensure complete wetting. In the other case, foaming may be controlled by adding an antifoam and/or increasing the viscosity of the vehicle. It is useful to record here the essential requirements for an antifoam.[7]

1. It must be immiscible, but dispersible, in the foaming system.
2. It must have a lower surface energy than the foaming system.
3. It should spread readily on the foaming liquid for optimum action.

The use of antifoams can be tricky since many antifoams are anti-wetting agents in solid/liquid systems, so that a vicious cycle of alternate additions of anti-foam and wetting agent can occur. Usually an optimum system can be devised. The author has found M.S. Antifoam "A" to be useful and also water-insoluble but dispersible polyethylene glycol esters and ethers, particularly when used with water-soluble non-ionic wetting agents.

Crystal growth in suspensions

Whilst it is theoretically possible in suspensions of solids for the larger crystals to grow at the expense of the smaller, this effect is only significant for large differences in particle size and for relatively large interfacial energies.[8] Generally, in pharmaceutical systems, under normal storage conditions, crystal growth is the result of decomposition, as in aqueous suspensions of aspirin when crystals of salicylic acid grow, or of change of crystal structure to a thermodynamically more stable form, as may occur in aqueous suspensions of cortisone and probably other steroids.[9] If crystal growth does occur, the system should be examined for these possibilities and, if possible in the latter case, the solid produced in a crystal form stable in the vehicle used.

Quality control of pharmaceutical suspensions

Frequently specifications for suspensions are phrased thus—in a certain time "Sedimentation should not be greater than . . ." — the purpose of the test being to prevent products being sent out which will clay on standing. Clearly a finely-divided deflocculated system could pass this test and yet give much trouble later. A much happier wording might be that in a certain time "sedimentation should not be less than .... or more than .... leaving a substantially clear supernatant liquid." This test specifies a controlled degree of flocculation.

A further test that is sometimes applied to suspensions is the degree of sedimentation after centrifugation in an effort to obtain a quick answer to the long-term behaviour of the suspension. This type of test is unlikely to yield useful information in this regard, especially if the rate of centrifugation is great. Then, the centrifugal forces may be great compared with the forces causing flocculation. The end-result is a close-packed sidiment irrespective of the degree of flocculation of the starting suspension. Carefully-timed controlled rate centrifugation may give a measure of the flocculative forces by affecting the sedimentation bulk, but it is doubtful if such a test is ever necessary for pharmaceutical systems. Microscopic examination and sedimentation behaviour are simpler and more reliable tests.

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1. The solid particles may be flocculated by suitable additives.
2. The vehicle may be given a degree of rigidity sufficient to support the particles mechanically.

Flocculating agents have the effect of increasing $E_{s.L.}$ or reducing the charge and/or the degree of solvation of the solid surface. For example, deflocculated aqueous suspensions may be flocculated by addition of a small amount of cetrimide or other quaternary wetting agent because the first layer of wetting agent forming on the particles is oriented carbon chain outwards.[1] This first layer is very firmly bonded to the solid surface and is not readily removed by washing. Further addition of cationic produces progressive degree of deflocculation since a second layer of cationic is adsorbed polar end outwards. By controlling the particle size of the solid and the input of cationic agent, it is possible to produce a suspension with the desired degree of flocculation. In general, if an amphipathic surface active agent is adsorbed at a solid-liquid interface with its non-polar end oriented towards a polar solvent, or with its polar end towards a non-polar solvent, flocculation is possible. For example, procaine penicillin is deflocculated and "clays" in arachis oil, but addition of a small amount of *Tween* 80 gives a "non-claying" flocculated suspension because the *Tween* is absorbed with the polyoxyethylene chain oriented towards the oil.[6]

Use of gelling agents

The use of bentonite in calamine lotion to produce a vehicle with some degree of mechanical rigidity has already been mentioned. In general, if the thixotropic force or yield point of the vehicle is greater than the weight of the particles, suspension of a deflocculated solid is possible. For example, procaine penicillin may be suspended in arachis oil or mineral oil gelled with aluminium stearate. In the case of the arachis oil gel, some flocculation of the particles may also occur due to formation of amphipathic molecules by oxidation of the oil if it is exposed to air whilst the gel is being made. In these systems, the aluminium stearate forms a molecular lattice-work which gives the gel a certain rigidity at rest. Introduction of a small amount of a polar substance such as glycerol disrupts the lattice-work, the system becomes fluid and the procaine penicillin "clays."

Foaming in suspensions of solids

Foaming in suspensions of solids usually results either from the presence of unwetted fine particles or the low surface tension of the system.

In the case of solid-stabilised foams, it is necessary to increase the concentration of wetting agent to ensure complete wetting. In the other case, foaming may be controlled by adding an antifoam and/or increasing the viscosity of the vehicle. It is useful to record here the essential requirements for an antifoam.[7]

1. It must be immiscible, but dispersible, in the foaming system.
2. It must have a lower surface energy than the foaming system.
3. It should spread readily on the foaming liquid for optimum action.

The use of antifoams can be tricky since many antifoams are anti-wetting agents in solid/liquid systems, so that a vicious cycle of alternate additions of anti-foam and wetting agent can occur. Usually an optimum system can be devised. The author has found M.S. Antifoam "A" to be useful and also water-insoluble but dispersible polyethylene glycol esters and ethers, particularly when used with water-soluble non-ionic wetting agents.

Crystal growth in suspensions

Whilst it is theoretically possible in suspensions of solids for the larger crystals to grow at the expense of the smaller, this effect is only significant for large differences in particle size and for relatively large interfacial energies.[8] Generally, in pharmaceutical systems, under normal storage conditions, crystal growth is the result of decomposition, as in aqueous suspensions of aspirin when crystals of salicylic acid grow, or of change of crystal structure to a thermodynamically more stable form, as may occur in aqueous suspensions of cortisone and probably other steroids.[9] If crystal growth does occur, the system should be examined for these possibilities and, if possible in the latter case, the solid produced in a crystal form stable in the vehicle used.

Quality control of pharmaceutical suspensions

Frequently specifications for suspensions are phrased thus—in a certain time "Sedimentation should not be greater than . . ." — the purpose of the test being to prevent products being sent out which will clay on standing. Clearly a finely-divided deflocculated system could pass this test and yet give much trouble later. A much happier wording might be that in a certain time "sedimentation should not be less than . . . . or more than . . . . leaving a substantially clear supernatant liquid." This test specifies a controlled degree of flocculation.

A further test that is sometimes applied to suspensions is the degree of sedimentation after centrifugation in an effort to obtain a quick answer to the long-term behaviour of the suspension. This type of test is unlikely to yield useful information in this regard, especially if the rate of centrifugation is great. Then, the centrifugal forces may be great compared with the forces causing flocculation. The end-result is a close-packed sidiment irrespective of the degree of flocculation of the starting suspension. Carefully-timed controlled rate centrifugation may give a measure of the flocculative forces by affecting the sedimentation bulk, but it is doubtful if such a test is ever necessary for pharmaceutical systems. Microscopic examination and sedimentation behaviour are simpler and more reliable tests.

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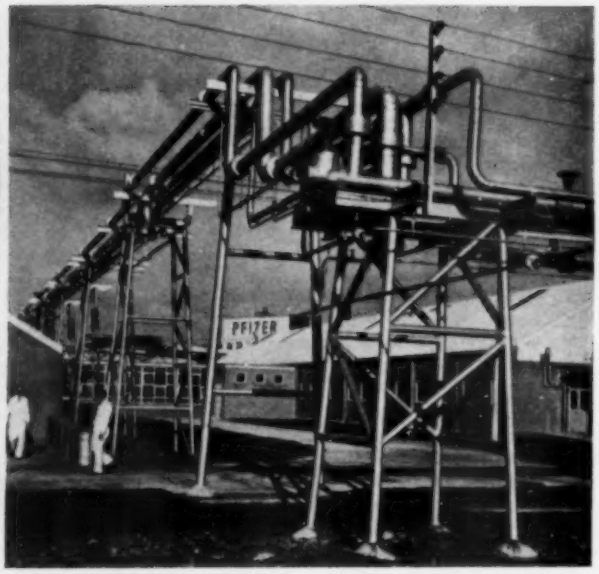
Pfizer's £1 Million Polio Vaccine Plant Now in



Left: Live virus inoculation. When the kidney tissue cells are ready, each flask is seeded with about 2 c.c. of one type of live polio virus. The flasks are again incubated for two to three days, in which time the live virus multiplies inside the cells and in doing so kills them, leaving a fluid rich in live virus. The fluid is harvested, inactivated, and after many searching tests, mixed with the fluid containing the other two types of polio virus to make the final inactivated vaccine. Right: The numerous overhead pipes carrying steam, water, gas and diesel fuel to the polio vaccine unit.

THE first batch of polio vaccine to be made by Pfizer Ltd., in their new plant at Sandwich, Kent, has now been released by the Ministry of Health. The batch comprises 163,000 doses. Other batches are in different stages of production and soon there will be a steady flow of vaccine from the new plant.

The plant

Pfizer decided to enter the vaccine field in September 1957. The new plant was started in October and 11 weeks after the first building—of 10,000 sq. ft. and containing 100 separate rooms—was finished. The whole plant was completed in the middle of February 1958. It covers about 30,000 sq. ft. and is divided into 200 separate rooms with air conditioning, sterile areas and many other of the complex systems required for the exacting process of polio vaccine manufacture. The whole project cost about £1 million.

The plant is now producing at the rate of 10 million doses of vaccine p.a., but this could be doubled. It is thus the biggest of the three British polio vaccine plants—the other two being those of Glaxo and Burroughs Wellcome. Pfizer estimate that it is now possible for the three British manufacturers to supply enough vaccine to immunise everyone in Britain up to the age of 40—about 20 million people. However, whether this will be done depends on the policy of the Ministry of Health.

Future requirements of vaccine

If recent medical opinion, that a fourth dose of vaccine should be given, the country's needs would be increased by a third.

But over 12 million children and adults have still not put their names down for immunisation. By the end of last year only about 60% of the parents of children from 6 months to 15 years registered their children for vaccination. Many have been waiting for adequate quantities of the British vaccine. This should now be available.

In the 15-25 age group, made eligible for vaccination by the Ministry of Health last year, the 350,000 registrations recorded so far represent an acceptance rate of less than 6%. Only about 19% of expectant mothers, who are very prone to severe paralysis if they contract the disease, have registered.

There are about 6 million people in the 15-25 age group and a further 9 million people, between 24-40 at present outside the scheme who, doctors say, ought to be immunised.

Pfizer are expecting to obtain a contract from the Ministry of Health to supply vaccine. The other two manufacturers, of course, have contracts. The problem of the Ministry is the disposal of present stocks of both British and imported vaccine. No further imports of vaccine are contemplated at present.

In announcing the release of their first batch of vaccine, Pfizer's chairman, Mr. Richard Fenton, appealed to the press to persuade the public to respond more vigorously to the offer of vaccination.

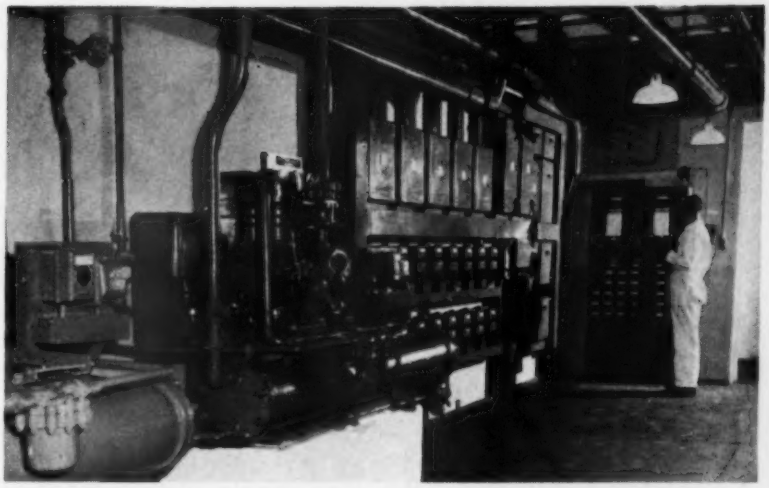
Teething troubles

The lag of 12 months between the starting of the plant and the acceptance of the first batch of vaccine was due to teething troubles resulting in initial batches being unsatisfactory and, of course, to the fact that the production cycle

Full Production

takes six months. Pfizer had no previous experience in this field and had to start from scratch to assemble a team of experts. Now 90 people are employed in the plant.

Mr. Fenton paid tribute to the help received from the Poliomyelitis Research Foundation of the South African Institute for Medical Research who, in January 1958, allowed the company's staff to work with them to gain experience. The technical staff of the Ministry of Health and of the Medical Research Council also gave advice. There was also co-operation with the parent company, Chas. Pfizer Inc. in New York, but in this case they too were working from scratch. In fact Pfizer in England produced



Electronically operated control panel of the vaccine unit plant room. This indicates also the temperatures in the seven incubators and two cold rooms, and should any piece of electrical or mechanical apparatus break down a warning light flashes on the panel. In the foreground is seen the air refrigerating unit.

Filling and sealing 1 c.c. ampoules with polio vaccine. The complete operation is carried out by one machine.

a successful vaccine before their American associates.

At Sandwich the Brunenders strain of polio virus is used. This is common practice in Britain. In the U.S. the Mahoney strain is used. Pfizer hope shortly to be able to announce the development of a vaccine substantially more potent than any yet produced.

Mr. Fenton told us that he did not expect his company to make a profit from polio vaccine for a long time. However, the company entered the field because it believes vaccines are important for a major pharmaceutical company. Now they have a large plant and have acquired experience in one of the most difficult vaccine manufacturing processes, they are equipped to make other vaccines and, probably, antisera.

ANTIBIOTICS MANUFACTURE

(Continued from page 150)

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British Congress of Cosmetic Science

Review of the Congress Papers

By Wm. W. Myddleton, D.SC.

The Congress, organised by the Society of Cosmetic Chemists of Great Britain, is being held from April 15 to 17 at University College, London. The subjects of the papers to be presented were chosen by a vote of the members of the Society, so they represent those aspects of cosmetic science of greatest current interest. A further report on the Congress will appear in our May issue.

SESSION I. ANALYSIS OF RAW MATERIALS

9.30 *a.m.*—12.30 *p.m. Thursday, April* 16

AT THE first morning session, the analysts open the proceedings with a paper by H. van den Dool (Polak and Schwarz) on **Analytical Methods in assessing the Value of Perfumery Raw Materials.** Here we have presented some deeply interesting exercises for the expert and some undoubtedly fascinating material for the non-specialist in the subject. Every student of organic chemistry is struck by the fact that purification of acetamide removes the mousy odour which he had assumed to be characteristic of the compound. He may also encounter the fact that personal idiosyncrasies affect in many individuals the appreciation of certain odours. Some, for example, cannot detect the odour of hydrocyanic acid but can detect the strange taste it induces when smoking a cigarette.

Now we are challenged by the suggestion, admittedly somewhat exaggerated, that perfumery chemistry is the chemistry of impurities. As an instance of this the author quotes trichloromethylphenylcarbinyl acetate, which before purification possesses a distinct rose odour, but which after purification is practically odourless. The interesting recital of the complexities and dilemmas encountered in the analysis of perfumery raw materials will fascinate the non-specialist in the subject and he will enjoy the performance of the analyst as he would a brilliant and artistic exhibition of skating on thin ice, very thin ice.

The author's own conclusion is that "the traditional methods of analysis give considerable insight into the functional groups present, and the lack of specificity inherent in these methods may be overcome by the modern chromatographic techniques, and in the near future by infra-red spectroscopic techniques. For the interpretation of his work a close co-operation between the analytical chemist, production manager and perfumer will be necessary, otherwise his figures will have no sense."

In the second paper, J. B. Stenlake and W. D. Williams (School of Pharmacy, Royal College of Technology, Glasgow) discuss **Ultra-violet Spectrophotometric Procedures in Essential Oil Examination.**

This is a paper of definite interest to the specialist; it deals with the measurement of the ultra-violet extinction coefficient before and after reduction of carbonyl groups with sodium borohydride. The method is here applied to the particular case of the estimation of α— and β— ionone in mixtures of the two forms. The results are in close agreement with theoretical values in prepared mixtures, except where there is a very large proportion of one of them.

The analysts continue the session with a paper by N. J. van Abbé (Genatosan Ltd.) on **Specifications for Raw Materials and Finished Products.** The author points out that the analysis of raw materials by the user is a costly undertaking. It must be remembered that many cosmetic houses turn out a variety of products, calling for a very wide range of raw materials.

The suggestion is put forward that the supplier's warranty or a certificate of analysis might suffice. One would be ready to accept this, especially for items supplied on the specification drawn up by the Toilet Preparations Federation. It is important however to bear in mind that mistakes are sometimes made, wrong labels are attached and wrong grades supplied from time to time. A minimum test should be applied to each delivery to eliminate possible errors of this kind. The paper will interest suppliers as well as users.

In the fourth paper, R. Barrington Brock (Townson and Mercer Ltd.) introduces **Trends in Mechanisation in Laboratories,** and explains how mechanisation can be introduced in stages. If made completely automatic, laboratory units would in some cases be rather costly, and the author asks how much the cosmetic industry would be prepared to pay. To illustrate how mechanisation increases costs, the author takes as an example a vacuum tester for moisture determination. A weighed sample is placed in a vacuum compartment, the lid is closed and sealed and the vacuum applied. The final reading of the moisture content appears on a dial when a needle is turned to a specified null-point. In the simplest form of mechanisation the dial could be mechanically turned to bring the needle to the null-point by a reversing electric motor. The operator would still be required to weigh the sample, place it on a pan, close the lid and switch on. At the ringing of a bell the operator would read the moisture content of the sample on the dial. This simple step in mechanisation would add about £100 to the price. In the second stage information as to the position of the dial could be fed on to a chart. This would mean that, in addition to the final figures for moisture content, the rate of drying could be observed. This would add a further £50-£80.

Another step would introduce a device for weighing the sample automatically, perhaps drawing the sample from bulk. Yet another step would introduce mechanism to unseal the vacuum, remove dried

V. O. E. Bryant

J. G. Feinberg

R. H. Marriott

N. J. Van Abbé

R. Barrington Brock

samples, introduce new weighed samples, and close and seal the container. These additional stages would greatly increase the cost.

When we consider the various forms of equipment which might with advantage be mechanised we can divide them into two groups. In the first the samples must be drawn and tested for control purposes near the site of manufacture of the product. There are other instruments which would be used only intermittently or for research investigations. Most of those in the second group would be excessively costly except for the larger organisations. The thesis will be developed later in conjunction with other considerations that the best interests of the industry and the community would be served by the establishment of a central research station for the industry to take charge of such equipment and to offer advice on the possibility of mechanisation of equipment in the first group for the use of individual firms.

The author discusses other forms of apparatus capable of conversion to complete or semi-automatic operation. It is pointed out that automation can save time by reducing manipulation and eliminating calculations and can give more accurate and reproducible results than a manual method so long as the electronic circuits remain in good order.

SESSION 2. ASSESSMENT OF FINISHED PRODUCTS

2 p.m.—5 30 p.m. Thursday, April 16.

L. H. Ovens (Consumer Research Division, Beecham Group Ltd.) opens the first afternoon session with a paper entitled **The Function of Consumer Testing in Product Development and Marketing.**

There is no disputing the author's statements that in the long run it is the consumer who determines the level of success of new or modified products and that no amount of advertising will repeatedly sell an unacceptable product. One must agree also that vast amounts of money may be lost by backing the wrong horse. From this point onwards there is room for disagreement with the practice of market research which involves " knocking on doors looking for elegible informants." Even this procedure leaves us in the position that " no consumer product research, however carefully planned, can absolve management from having to make decisions."

For the peace of mind of management and consumer alike it would appear more humane to try out a new or modified product by experimental marketing in a limited territory with sufficient local advertising to give it a reasonable start.

As a preliminary to market testing it is necessary to evaluate cosmetic performance by using panels under laboratory control. This apect is dealt with by D. H. Powers (Cosmetic Research Division, Warner Lambert Research Institute, New Jersey) under the title **Laboratory Tests as a Basis for Accurate Product Market Testing.** At the outset the author makes an arresting statement: " It is widely recognised that fancy or smart packages, clever and frequent advertising and efficient distribution all contribute tremendously to sales success. Also it is true, particularly in the cosmetic industry, that clever advertising can make a poor product far outsell a product with much better technical performance. There are numerous examples where " soap and water " in a fancy package has proved to be more financially rewarding than a scientifically formulated colloidal dispersion of submicroscopic particles of controlled molecular aggregation with low surface tension and high cos θ."

In equally strong terms the author enumerates examples of advertising which at the present time appear as a " rash of miracle ingredients " leading to the claims:

" supply the moisture that tensions and weather have stolen from the skin,"

" it puts back dew while removing grime,"

" it is a cosmetic which comes from the bottle and is applied to the soul creating beauty from inside out,"

" activates and normalises the skin,"

and so on.

" If we can accurately measure in the laboratory actual performance of creams, lotions and cosmetic products we can supply real performance claims for cosmetics in place of these miracle promotions," says Mr. Powers.

The American Society of Cosmetic Chemists has now set up six committees to study laboratory methods for evaluating shampoos, permanent wave lotions, aerosols, creams and lotions, deodorants and anti-perspirants, and face and body powders. The investigation aims first of all to draw up a short list of known methods of testing a given type of product and then to have these tried out in a number of different laboratories. Any test found to give reproducible results is then submitted to the Society as a tentative evaluation method published for comment and criticism in the *Journal* of the Society of Cosmetic Chemists. Twelve months later any method found satisfactory is to be published as an official S.C.C. test.

Tentative methods have already been published on antiperspirant and deodorant value and a method for determining the *p*H of shampoos. On panel testing the author expresses the view that if a user says that one cream cleanses better than another or leaves the skin softer, the value of her evidence is doubtful and the question can be asked, "How does she know that one cream has a better cleansing action than another? What is her method of

testing?" It is the duty of the laboratory, says the author, to devise methods to measure these things.

To show how tests of performance might be developed in the laboratory for shampoos, systematic measurements have been tabulated giving the percentage soil removal from keratin (wool) by 0·25% solutions of a large number of different detergents. A similar table gives the soil removal from keratin by 0·5% solutions of various shampoos, the *p*H values being recorded also. Other observations were conducted with the same materials but using alternatively tap, hard and sea water.

Since foaming power has a strong appeal the effect of sebum, hard and soft water on foaming power was measured. By an elaboration of this kind it is claimed that a surer foundation for consumer tests can be laid.

The third paper on assessment, by L. S. Adler (Unilever Ltd.), deals with **Product Evaluation from the Rheological Aspect.**

The rheological properties are a measure of the tactile properties of a product and their evaluation, the author claims, will provide the formulator with a quantitative assessment of what the consumer feels when he or she applies the product to the skin. If the rheological properties of a product have been accurately assessed before panel tests are applied, correlation between panel tests and rheological evaluation can frequently save much painstaking and unnecessary labour.

Care and circumspection must be exercised in the choice of instrument used for any particular rheological problem.

The first day closes with a discussion introduced by E. J. Moynahan (Dermatological Department, Guy's Hospital) on **The Patch Test in the Diagnosis and Prevention of Cosmetic Dermatitis.**

After presenting a statistical study of the incidence of dermatitis of various kinds the author concludes that cosmetics are not responsible for much skin trouble and that cosmetics are among the least harmful substances to which we are exposed in our daily lives. Patch testing plays an important part in making sure that products applied to the skin in cosmetics are harmless, and they also assist in identifying the cause of any dermatitis suspected to be of cosmetic origin. Details are given of the method of applying the patch test and the reading and interpretation of the results.

SESSION 3. MANUFACTURING OR PROCESSING

9 30 a.m.—12.30 p.m. Friday, April 17

The second day of the congress opens with a session on factory procedures. V. O. E. Bryant (County Laboratories Ltd.) introduces **Heat Transfer in Cosmetic Manufacturing Processes.**

The author rightly makes no apology for mentioning a number of elementary facts which are frequently overlooked. He may be assured that more elementary facts than he mentions are vey often ignored. For example, the effect of controlled cooling on the quality of cosmetic products is seldom realised and in many cases the means of rapidly cooling, providing adequate stirring to improve heat transfer from a low heat-conducting mass of high viscosity, and the efficient application of the cooling medium, are not available and have never been properly considered.

The problems of economical heating and cooling are, fortunately, less important than the quality of the product, for heat losses are, in many places, outrageously high. Sometimes however these losses are insignificant when compared with the losses occurring in badly designed space heating and ventilating. In a further aside one might mention the very common defects in the heating and ventilating of laboratories. These defects lead to the reckless opening of windows with much heat loss and the introduction of draughts which play havoc with observations affected by temperature change and carry into the laboratory much undesirable dust and dirt.

The author gives much practical information which, if studied and applied, can do a lot to remedy expensive faults.

A paper by E. S. Sellers and W. L. Wilkinson (Dept. of Chemical Engineering, University College of Swansea) on **The Effect of Rheological Properties on Mixing and Heat Transfer** is more theoretical and of greater interest to the specialist designer of plant.

The prospect is offered of extending the calculation of power requirements in mixers and of area requirements in heat exchange systems from Newtonian to non-Newtonian fluids. The prospect is not, however, an immediate one, for in many cases cosmetic materials require cooling after emulsification. The emulsions are not only non-Newtonian but are also undergoing changes which lead to alteration in particle size and distribution of particle sizes. These complications are superimposed upon those arising from the fact that the system is non-Newtonian. For some time it will apparently be necessary to solve the problems involved by direct experiment.

There is so much to be said by way of comment on a paper in the final session that no further mention will be made here of the paper of K. F. Larking and J. E. O. Mayne (Ministry of Supply Australia and Dept. of Metallurgy, University of Cambridge) on **Corrosion of Iron and Aluminium,** and the paper by D. M. Wylie (T. B. Ford Ltd.) on **Fundamentals of Filtration.**

SESSION 4. BIOLOGICAL ASSESSMENT

2 p.m.—5 15 p.m. Friday, April 17.

Cosmetic chemists have for many years been deeply concerned to learn more about the structure and reactions of the skin, the changes that take place in ageing, and how cosmetics may be formulated to minister to the well-being of the human organism. Evidence of this concern is to be found in the papers read before the Society or printed in their Journal. If more evidence were required it could be found in the papers delivered to the Congress of 1959. It has long been held that the cosmetic chemist himself cannot deal with all the complicated problems of cosmetic science.

There was a time when the chemistry student at the university had the inclination and the means to scan wider horizons than those bounding his special subject. Many found it possible to study also more than the introductory stages of biology, physiology, anatomy and histology and to carry out some measure of research work in these regions. Such men might become good cosmetic chemists. Economic conditions have now put an end to much of this exploration, and so teams of biologists, physiologists and so on must now be recruited to tackle the problems awaiting attention.

The recruitment of good and

devoted workers is at the present time made difficult by the general distrust of the ultimate use that will be made of their work, fostered by the way in which the products of the industry are presented to the public. W. S. Bullough (Dept. of Zoology, Birkbeck College, University of London) in his paper on **The Present State of the Cosmetic Industry** describes the publicity lavished on the work of the cosmetic chemist as brilliant. Dr. Bullough, a scientist looking in from the outside, can discern something radically wrong with the industry:

> "The crux of the matter is simple: the cosmetic industry is in fact dispensing treatment for a living organ, the skin, and yet the dispensing is being done by those who have little or no conception of the problems which are really involved."

The matter was presented in somewhat the same terms by a cosmetic chemist two years ago (*Chemical Products*, February 1957).

Dr. Bullough, "looking in from the outside," is thus in the position of the experimental zoologist who, carrying out observations on the behaviour of monkeys, kept them in a room in which various tests were carried out. Leaving the room one day he thought he would watch them for a while unseen by them. Applying an eye to the keyhole he was surprised to find himself gazing into the intent eye of a monkey closely applied to the other side of the hole.

It appears to be an inevitable conclusion that to do anything adequate to remedy the state of affairs it will be necessary to set up a research station to serve the whole industry. Few firms are able to face the expense of assembling a team of workers. In fact it would not be justified or advantageous for the effort to be left to individual units in the industry, for it would maintain the present stifling secrecy which surrounds scientific work on cosmetics.

A lead in the right direction has been given by the Toilet Goods Association of America. A Scientific Section was set up a number of years ago and the results of their work, much of it concerned with the behaviour and reactions of the skin and its appendages, are published at intervals in the valuable Proceedings of the Scientific Section of the Toilet Goods Association, a journal with a world-wide circulation.

It has already been suggested that other work would be carried out by such a research organisation, for example in exploring the possibility of automation both in the laboratory and in the factory, in the design of efficient plant and so on.

Other papers to be presented in the fourth session on Friday are:

F. J. Ebling (Dept. of Zoology, Sheffield University) on **Recent Advances in the Biology of the Skin,**

J. G. Feinberg (Bencard Allergy Research Unit, Beecham Research Laboratories Ltd.) on **Cosmetics, Allergy and Skin,** and

R. H. Marriott (County Laboratories Ltd.) **Cosmetics as a Factor in Civilisation.**

MULTICOLOURED SOAPS

Soap consisting of several parts which differ in colour, smell and ingredients and which are made to fit into each other and can be joined mechanically is the subject of a new German patent application 23f, 3.R445. The invention enables the parts to remain separate and distinguishes the new soap from the older types of multicoloured soap, in which the different layers flow into each other under hydraulic pressure.

In the new soap the layers are joined by means of grooves and tongues, or the whole piece consists of an outer case and one or more cores. A white medical soap, for instance, may have a yellow core containing 5% lanolin and a red core containing 1-2% sublimate. Embossed surfaces may help to keep the parts in position, or pins or blades made of Celluloid, Bakelite or some similar material and perhaps carrying an advertisement may be used for this purpose. Such advertisements are likely to be effective, as the pins and blades remain behind when the soap is used up, and the user is bound to look at them.

The parts are made separately under pressure as long strings with fitting profiles, the strings are then united, cut and pressed into the desired shape.

The patent specification is published in *Seifen—Oele—Fette—Wachse* 1959, **85,** (5), 109. Illustrations show strings of different types—separate and joined—as well as a machine for making the new soap.

Industry's Publications

Industrial vacuum cleaner. An illustrated leaflets available from Sturtevant Engineering Co. Ltd. gives details of their *Six-X-Three* industrial vacuum cleaner which has a three-stage turbo-exhauster and is stated to be exceptionally mobile.

Laboratory fittings. A 63-page illustrated catalogue from A. Gallenkamp and Co. Ltd. describes their wide range of laboratory furniture and equipment fittings. These include vacuum pumps, waste fittings and traps, sinks, gas plant and air compressors, as well as bench assemblies in a variety of materials and combinations.

The Chemist and Druggist Year Book 1959. This useful reference book is made up of a trade directory and buyers' guide (incorporating a trade name index) covering a wide range of plant, pharmaceuticals, chemicals, toilet preparations and sundries, 50 pages of factual information intended mainly for retail pharmacists, and a diary. The trade directory lists about 1,200 firms.

Applications of EDTA. British Drug Houses Ltd. have published a 106 pp. book describing the analytical applications of diamino-ethane-tetra-acetic acid. The first chapter describes EDTA and its complexes and subsequent chapters deal with indicators for titrations, the use of masking and demasking agents, end-point detection, determination of metals, anions and water hardness, and analytical applications of other complexones. There are 10 pp. of references. *Analytical Applications of Diamino-Ethane-Tetra-Acetic Acid*, by T. S. West and A. S. Sykes, price 4s. 6d., is available from The British Drug Houses Ltd., B.D.H. Laboratory Chemicals Division, Poole.

Nitrogen. This is the name of a new quarterly magazine published by the British Sulphur Corporation Ltd. The Chairman of the Corporation, Mr. G. E. Wildman-Lushington, says: "At a time when a substantial measure of surplus capacity is appearing in some quarters and when all sectors of the industry are subject to far-reaching changes, this new magazine will pay close attention to technical and economic developments affecting the production and consumption of nitrogen and its derivatives throughout the world, providing an impartial service to producers and consumers alike." The publication measures 7¼ by 9¼ in. and the first issue contains 60 pages. The subscription is 10 guineas p.a.

Pest Control Chemicals

By D. P. Hopkins, B.SC., F.R.I.C.

Nematocides • New insecticides • Weed control developments Black spot disease control • Pyrethrum and water supplies • Microbial insecticide • Parathion hazard

The nematode problem

SCOTTISH research on potato eelworm control was discussed in the last Report (see MANUFACTURING CHEMIST, February 1959). A U.S. paper[1] emphasises how widespread and costly the nematode problem is; severe rotation of crops is still the main form of control because it is only in special circumstances that soil fumigants can be economic. Total annual losses to nematodes in the U.S. are variously estimated at between 500 million and 1,250 million dollars.

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For many years the main chemical approach to nematode control has been soil fumigation. Almost 50 years ago, in the infancy of modern pest control by chemicals, the extensive dosing of the soil with carbon bisulphide was claimed to be the sovereign remedy for nematode infestation. At that time, however, the magnitude of the nematode problem was hardly realised. If a low-cost nematocide is to be developed, it seems necessary to break away from the idea of a volatile soil fumigant; even if such a material is itself fairly inexpensive, its cost of application per acre will be high. Admittedly, the prospects of a non-fumigant attack seem less hopeful, but further research may present a different picture.

A new American soil fumigant is *Mylone*, or 3,5-dimethyl tetrahydro-1,3,5,2-thiadiazine-2-thione, for use as a pre-planting control for nematodes, some weeds, and soil fungi.[3] It would seem to enter the seed-bed treatment field, and this is, of course, a high-cost field in which several established soil fumigants are used. *Mylone* is plant toxic, and until more is known about its long-term toxicity it cannot be recommended for edible crops. On the other hand, its short-term toxicity appears to be low. It is not readily absorbed by the skin and special protective clothing is not needed for handling.

New insecticides

Dibrom, or o,o-dimethyl-o-(1,2-dibromo-2,2 - dichloroethyl) phosphate, has a wide range of contact toxicity to insects and low residual activity.[3] It has the general toxicity properties of most organo-phosphorus insecticides and the usual precautions for these substances must be applied. Apparently less toxic than most organo-phosphorus insecticides, *Delvan*, or 2,3-*p*-dioxanedithiol - s - s - bis (o,o-diethyl phosphorodithioate), is both a miticide and insecticide; it is approved for use as the former for many crops, but as yet only for a few crops as the latter. It is also a promising livestock pesticide, and has been approved for use against brown ticks on dogs.

Phosphamidon, or 2-chloro-2-diethylcarbomoyl-1-methylvinyl dimethyl phosphate, is a new systemic effective against sucking and chewing pests.[3] Aphid control has been outstanding. It may be soil-applied to enter plant systems via roots or bandage-applied to trunks of trees. It has no phytotoxicity with most plants at the application dosage rates. It is apparently as fully toxic as most organo-phosphorus substances. It is corrosive, and also decomposed by some metals and alkalies; it must be packed in glass or plastics and kept protected against moisture. PRD, or 3,4-dichloro tetrahydrothiophene 1,1-dioxide, is a new nematocide still only in experimental use; it is acutely oral-toxic. It would seem to be a promising nematocide but one with specialised rather than general effectiveness.

Weed control developments

An additive to reduce spray drift troubles has been developed.[3] It is a dispersion of oil particles in water and the thick creamy consistency obtained gives sprays greater capacity to cling to foliage and branches, while mist emission during spraying is said to be prevented. The emulsion is called *Inverton* 245 and it contains 2,4,5-trichlorophenoxyacetic acid.

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field work before it can be generally recommended. The bean's immunity to damage seems less on sandy soils than on clay soils.

Selective chemical weedkillers for cereals now total ten and the choice of the most suitable in any given cereal-weeds situation has become complicated. On this subject another British contribution[6] is an up-to-date and exceedingly valuable reference. It deals with the newer (since 1955) cereal weedkillers, CMPP, SMA (sodium monochloroacetate) and CP-1815, now known to be a mixture of MCPA and 2,3,6-trichlorobenzoic acid. Woodford stressed the need for specialised advisory services now that chemical weed control had become a far more complex subject; manufacturers have already built up advisory services, but the N.A.A.S. has yet to follow suit in

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Phenyl mercuric chloride for black spot disease of apples is discussed in a recent paper based upon field work in Australia.[7] The history of previous and not wholly satisfactory control treatments is reviewed, *e.g.* with Bordeaux mixture followed by lime sulphur and copper-lime-arsenite mixtures. The weak spot in the black spot fungus's life cycle is the period between harvest and leaf-fall when the infection is confined to the tree and not yet spread to the leaves. Phenyl mercuric chloride is able to give 95% reduction without damaging the tree,

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Woodford's survey also mentioned simazine (see these Reports, MANUFACTURING CHEMIST, 1957, **28**, (10), 474) or 2-chloro-4, 6-bis-(ethylamino)-*s*-triazine, a persistent near-total weedkiller to which some crop plants seem relatively immune and to which maize is wholly immune. Field beans have nearly as much immunity as maize. The selectivity, so unusually specific, is due to enzyme systems in the immune or near-immune plants which can break down simazine when it enters the plant system and before it can exert phytotoxic effects. Simazine is very water-insoluble and small rates per acre persist for more than a year in the soil. Crops which can benefit from this weedkiller mentioned by Woodford are, besides maize and field beans, asparagus, blackcurrants, and some shrubs and trees. The use of simazine for weed control with beans requires more field work before it can be generally recommended. The bean's immunity to damage seems less on sandy soils than on clay soils.

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A bacillus for insect control?

Large-scale field tests during 1959 are planned for what is called a microbial insecticide.[3 9] The spore-forming bacterium, *Bacillus thuringiensis* Berliner, has a wide range of susceptible insect hosts, and it is said that it can be applied in dust or spray forms with conventional equipment. Industrial production by fermentation methods would appear to have been initiated at least on a pilot-scale. Its virulence is not lost with repeated artificial growth, but it is harmless to warm-blooded animals so that its use should be free from problems of dangerous residues. Somewhat extensive claims or hopes have been indicated already, but these may be over-optimistic. The paper referred to above[9] puts the prospects of this first microbial insecticide into per-

spective and warns against regarding it as a panacea.

A parathion hazard

The toxic hazards of insecticides that can be absorbed by the skin are not confined to the operations of spraying or dusting. Residues of such insecticides on the stems and foliage of treated plants are potentially a risk to workers who must frequently handle the plants in other cultivation work. Thus, in a commercial tomato nursery, staff may be handling many hundreds of plants per day, and residues of an organo-phosphorus insecticide could be cumulatively absorbed. A recent British paper[10] reports a thorough investigation of this risk, with parathion as the test insecticide and tomatoes and cucumbers under glass as the test crops. "Smoke" and aerosol methods of parathion application were tested. It was found that there was greater contamination of hands (or gloves) with parathion-treated tomato plants than for similarly treated cucumber plants, and this seems due to the hairy surfaces of tomato leaves and stems. The highest contamination risk was when tomato plants were handled soon after an aerosol application. Nevertheless, the amounts thus picked up on the hands are unlikely to be hazardous; the quantities involved are minute, and the inevitable soiling of the hands through tomato plant handling means that hand-washing will be fairly frequent, further reducing contamination. This reassuring conclusion is supported with copious data. However, this wide measure of safety applies only to normal rates and to normal methods of parathion application. With much increased rates of use or under different conditions of distribution, the contamination risk may be higher.

Dust kills insects

Silica dusts that dehydrate insects mark a new approach to pest control in the U.S.[11]

The dusts adsorb the waxy or oily layer that covers insects' bodies. Deprived of this coating, needed to retain vital body moisture, the insects "dry" to death. Since no biochemical action is involved, insects probably will be unable to develop immunity. Non-toxic to man and animals, the dusts retain their effectiveness indefinitely. Under laboratory and field test conditions, two synthetic dusts, a silica gel and a silica aerogel, proved to be the most outstanding of a large number of adsorptive compounds tested. A little of either goes a long way. Only a small quantity picked up by an insect is sufficient to cause death within a short time. The particles measure about 0·02 micron in diameter.

Two other developments are claimed to show "tremendous" promise in coping with the $4,000 million worth of damage caused each year by insects and vermin in the United States. One is the development of methods to inject insect populations with diseases fatal to the insect but harmless to other living creatures; the other deals with advancing or retarding the normal life cycle by hormone treatment, with fatal results.

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ANTIBIOTICS

By R. Levin, F.P.S.

Food preservatives • Anti-cancer tests • Plant protection with antibiotics • Ringworm treatment • Penicillin-resistant staphylococci • India's antibiotic industry

Food preservation

MAINTAINING raw fish in good condition is a problem which has always faced the fish industry. Ice and cool storage is the only satisfactory means of preservation so far, but the period of preservation is still relatively short so that the fish must be moved quickly from port to shop. Addition to the ice of a small proportion of chlortetracycline has been described and this step is claimed to improve the keeping quality of the catch. At the Torry Research Station, Aberdeen, tests have been under way for some time to establish whether the incorporation of that antibiotic did improve the keeping quality of fish and what concentration, if any, of antibiotic was present after cooking.[1] Codling stored in ice containing chlortetracycline (5 ppm.) were sampled at two-day intervals and the antibiotic content of the skin and tissues determined. A striking but unexplained observation was the marked difference in the concentration of antibiotic between the two sides of the fish, *i.e.* the side lying uppermost always contained considerably more antibiotic. The greatest concentration was found in the skin, little or no antibiotic appeared to penetrate to the deep flesh—

Skin
- *Uppermost:* 1 p.p.m. (2nd day) to 12 p.p.m. (22nd day)
- *Underside:* 1 p.p.m. (18 to 20 days)

Subcutaneous layer
- *Uppermost:* 0·3 p.p.m. (2 days) to 4 p.p.m. (20 days)
- *Underside:* 0·3 p.p.m. (10 days) to 1·5 p.p.m. (22 days)

Deep flesh
- *Uppermost:* 2 p.p.m. (22 days)
- *Underside:* 0·2 p.p.m. (22 days)

Washing the fish to remove surface slime removed about 20% of the antibiotic present, while experiments on the effect of cooking showed that following steaming or boiling there was no residual antibiotic in the tissues, although half of the original activity remained in the skin. Baking in the oven at 190°C. for 15 min. produced surprisingly little reduction in the antibiotic content of skin and flesh.

The use of antibiotic-ice for the preservation of fish has not yet received approval, even in the United States. The American Cyanamid Co. is reported to have sought permission from the Food and Drug Administration last year, but

this was not accepted on the ground that more research was needed on the residue problem in uncooked fish. Since that rejection, Cyanamid has been hard at work gathering data on chronic toxicity based on tests carried out in dogs and rats fed with various percentages of the antibiotic in their diets. Having concluded from these tests that chlortetracycline could be consumed without harm at a level of 5 p.p.m. the company have recently submitted a further petition. This time the F.D.A. have accepted the petition for study and in conjunction with the Department of Agriculture are now checking the data supplied. An F.D.A. official apparently stated that if the research data is found to support the company's conclusions, clearance for the use of the antibiotic may be expected. That decision may have far-reaching implications in the preservation of other food such as fresh fruit and vegetables. It has already been shown that dipping raw salad vegetables in a solution containing oxytetracycline 250 or 500 p.p.m. will prevent spoilage for up to 48 hr. at 30°C. or 12 days at 5°C.[2]

The use of chlortetracycline or oxytetracycline for the preservation of poultry carcasses is permitted in the U.S.A. In Britain the advantage of adding these and other antibiotics to table poultry is being studied.[1] The first evidence of spoilage in uneviscerated carcasses is "greening," which occurs under the vent and on the abdomen. This is believed to be due to the diffusion of hydrogen sulphide produced by bacteria in the gut during storage; reaction with pigments of the blood and muscle produces a green pigment—sulphæmoglobin. Greening is currently retarded by the prompt cooling of the carcase immediately after slaughter.

The addition of oxytetracycline 50 p.p.m. to the drinking water taken by the animals shortly before death has been found to delay the onset of greening, extending the shelf-life of the bird in prime condition by 30% at 15°C. The time taken for greening to spread in treated birds is increased by 80%. In the case of eviscerated poultry held at chilling temperatures, spoilage is due particularly to psychrophilic bacteria which grow on the surface and on the flesh lining the visceral cavity. The shelf-life of such birds has been found to be increased by up to three weeks at cool temperatures if chlortetracycline is added to the tanks of ice-slush used for cooling the carcasses. Refrigeration appears to be a necessary component, since without it the antibiotic failed to produce any significant extension of shelf-life.

Anti-mitotic antibiotics

Typical of the fervour with which American antibiotic manufacturers are contributing to the search for anti-cancer agents is the work proceeding at the John L. Smith Memorial for Cancer Research, Maywood. The Memorial, which is associated with Pfizer is screening antibiotic broths for anti-cancer activity. Soil samples are received at Maywood from all over the world and these are examined to identify the micro-organisms present. Promising looking organisms are put to work fermenting broths which will subsequently be injected into animals with implanted cancer. Broths reported to be active are then fractionated to isolate the active principle or principles. Isolated compounds are sent to a pilot plant for larger scale production, whereupon the larger quantities thereby obtained are submitted for pharmacological investigation. A large proportion of the relatively few compounds that proceed to this stage have to be rejected because of unduly high toxicity. From this programme Pfizer hope to find about six compounds each year which are good enough for clinical trial. Of course, it is appreciated that the chances of finding even six promising compounds are low, but optimism apparently prevails.

Treatment of plant disease

The use of antibiotics, especially streptomycin and the broad spectrum antibiotics, for the treatment of plant disease has been known for some years. Penicillin, griseofulvin, chloramphenicol, chlortetracycline, streptomycin and oxytetracycline have all been shown to be absorbed and translocated to the skin and leaves following application to the roots. Comparatively little study has been made on whether antibiotic substances are absorbed by the leaves and other tissues and translocated *downwards* to other parts of the plant. In a contribution from the Merck Research Laboratories, Gray[3] provides evidence on this point and moreover shows that the absorption of antibiotics by the leaves is by no means universal among antibiotics. Those tested were applied to the foliage either by spray or by placing a single primary leaf in the antibiotic solution for several days. Transport of the antibiotics out of the leaves both up the stem to new leaves and down to older leaves and roots was traced by assaying portions of the plant. Antibiotics tested by the author included streptomycin, penicillin, tetracyclines, chloramphenicol, neomycin, bacitracin, viomycin, streptothricin and pleocidin. The results of spraying a 1% solution showed that only streptothricin and pleocidin were readily absorbed and transported from the leaves of bean and tobacco plants. When the same antibiotic solutions were applied by dipping a single leaf for several days, many of the other antibiotics were also absorbed. Dowler and Goodman[4] found evidence that streptomycin is translocated downwards when a solution containing 1,000 units/ml. was brushed on proximal or distal portions of leaves of *Coleus* sp. Although the antibiotic was detected in the stem, no activity was found in the roots.

In a therapeutic test Gray sprayed the primary leaves of bean plants previously inoculated with *Xanthocomonas phaseoli* with streptothricin or pleocidin. The plant subsequently showed no evidence of common bacterial blight. The author demonstrated that the downward transport of streptothricin was principally in the xylem.

Oral treatment for ringworm?

Fungous infections are rarely life-threatening and, with few exceptions, have therefore never been classed as serious disease. However, figures published by the U.S. Office of Vital Statistics show that there were 351 deaths from mycotic infection in the U.S.A. during 1955. Some part of these fatalities are undoubtedly due to infections caused by the yeast *Candida albicans*, which occasionally result from the administration of broad-spectrum antibiotics. Fortunately the antifungal antibiotic—nystatin—is now available for the treatment of many of those otherwise uncontrollable infections. The figures for fungous infection fatalities are no indication of the widespread distribution of mild skin conditions attributable to the presence of fungal parasites,

the successful eradication of which is frequently still unattainable.

Although more than a score of potent antibacterial antibiotics are currently available, the number of antibiotics active against fungi is remarkably low. This may be due to the eagerness in early screening programmes to isolate substances with activity against infectious bacteria. Those with antifungal activity have often been toxic and *in vivo* tests frequently failed to confirm expectations derived from laboratory results.

Griseofulvin, the metabolic product of a number of species of *Penicillium* first isolated in 1939, has recently achieved a prominence as a possible addition to the small group of substances already available for the treatment of fungal disease. The substance is markedly fungistatic *in vitro* and is reported to have low mammalian toxicity. Armed with that information and the knowledge that little or no work has appeared describing the systemic treatment of ringworm, Gentles[5] gave griseofulvin by mouth to a number of guinea-pigs with induced *Microsporum canis* infection. Dosage at the rate of 60 mg./kg. daily was started after the lesions were well developed. Within four days of the first dose beneficial effects were seen. The hair which grew during the course of treatment was found, on histological examination, to be entirely free of the micro-organism. Lauder and O'Sullivan[6] used griseofulvin in the prevention and treatment of experimental ringworm in cattle. When the antibiotic was given by mouth at the daily rate of 60 mg./kg., the establishment of artificial infection with *Trichophyton verrucosum* was entirely prevented. When the control group, which had developed mature ringworm lesions, were given the antibiotic therapeutically, all histological evidence of infection disappeared within two weeks. After three weeks new hair was growing and the typical ringworm crusts were no longer present. In a further communication, Gentles and co-workers[7] have postulated that griseofulvin is able to penetrate into the hair follicle, becoming incorporated into the newly formed keratin of emerging hair shafts. The hypothesis was tested by removing hair from a group of guinea-pigs which had received 23 consecutive daily oral doses of griseofulvin 30 to 40 mg./kg. Water washing followed by solvent extraction of the hair each produced approximately similar quantities of the antibiotic. The authors concluded that whilst some part of the griseofulvin enters the hair follicle another portion appears to be excreted through the skin, adhering to the external surface of the hair follicle. In a preliminary communication Williams *et al.*[8] have suggested that oral griseofulvin may be effective in the treatment of superficial fungous infections in man. They gave an arbitrary dose of 0·5g. four times daily as the only treatment to nine patients with *Trichophyton rubrum* infection of the skin or nails. The patients reported a rapid control of itching, characteristic symptoms of the disease began to disappear and within two weeks it became difficult to find the fungus in scrapings of the affected area. There was no evidence of side-effects. The authors believed their results to suggest that griseofulvin may be of therapeutic value, but were careful to add that many more months of trial will be required before a proper appraisal can be made.

The problem of the resistant staphylococcus

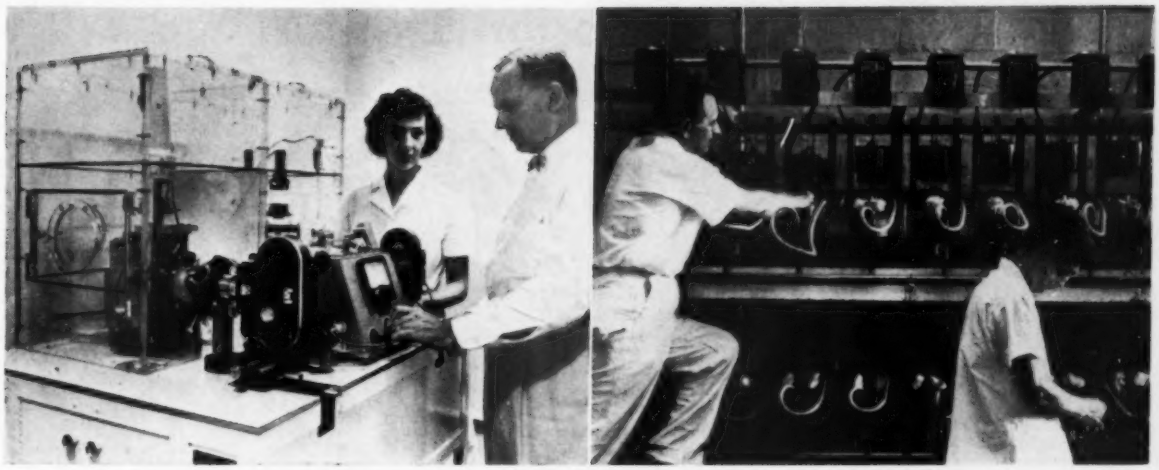
Resistant staphylococcal infections have been a prime topic of interest during recent months. A Report by a sub-committee of the Central Health Services Council under the chairmanship of Lord Cohen of Birkenhead draws attention to the prevalence of staphylococcal disease in hospitals and discusses methods of prevention. The suggestion that antibiotics are responsible for the problem is not supported by the authors of the Report, who emphasise that the ubiquitous staphylococcus was well known before the antibiotic era. Nevertheless, that the indiscriminate use of antibiotics can add to it is noted and hospital physicians are invited to keep certain antibiotics known to be effective against staphylococci (*e.g.* erythromycin) in reserve and to withhold the use of other antibiotics where possible. The resistant staphylococcus, a universal problem, is being studied in many parts of the world. It provided the subject of a panel discussion during the 1958 Symposium on Antibiotics held in Washington, where it was agreed that more than just a new and better antibiotic was needed—medical authorities are recognising the part that bad hospital housekeeping can play.

For the treatment of a fulminating infection due to staphylococci resistant to the major antibiotics the panel favoured the use of vancomycin, kanamycin and ristocetin. Only the last named is currently available in Britain. Antibiotic resistance will be discussed also at the International Symposium on Antibiotics due to be held in Prague, Czechoslovakia, on May 18-23 next, and at a Symposium sponsored by the Italian Society of Obstetricians and Gynecologists to be held at Perugia, Italy, on May 1-3.

The staphylococcus was once held to be sensitive to penicillin, but the proportion of the staphylococcal population resistant to the antibiotic has increased, particularly in hospitals. Consequently penicillin is often ineffective in staphylococcal infections. Penicillin-resistance in the staphylococcus is believed to be due to the ability of resistant organisms to produce an enzyme *penicillinase* which is capable of producing the rapid chemical degradation of the antibiotic with the subsequent loss of its antibacterial activity. To counter this effect Sollman and Streatfield[9] have suggested the administration with the penicillin of a penicillinase-*inhibitor*. Various compounds were tested, *in vitro*, by the authors, for the ability to inhibit penicillinase production in a penicillin-resistant pathogenic strain of *Micrococcus pyogenes* var. *aureus*. The compounds tested included quinine, quinacrine, chlorquine, trypsin, chymotrypsin, xylocaine, sulphathiazole, sulphadiazine, sulphanilic acid and *d*-penicillamine. Of these only trypsin, chymotrypsin and quinacrine were considered sufficiently active to warrant *in vivo* study.

Antibiotic production in India

In 1947, at the time of independence, India was a country with little experience in the pharmaceutical or chemical industry. The new Government was keen to expand industrially in many fields, therefore the development of an indigenous antibiotic industry had special problems. How and when these were met and tackled and the remarkable progress made once the preliminaries were completed is told by Raja.[10] The author describes the creation and development of the only Indian antibiotic manufacturing company in the first issue of an English language scientific



The Search for an Anti-Cancer Antibiotic

Left: Photographing cancer cells. John L. Davenport, director of the John L. Smith Memorial for Cancer Research at Maywood, N.J., checks exposure in a study of the growth of cancer cells by high magnification, time-lapse motion pictures. The microscope and camera on the left record the growth of the cells in a nutrient medium; those on the right the growth of cells in an identical medium to which a new anti-tumour substance has been added.

Top right: Antibiotic broths which have been found to show some anti-tumour activity are produced in quantity in this bank of fermentors.

Right: It takes four hands to hold a mouse for tumour implantation.

periodical on antibiotics published by that company.

As early as 1942 a committee set up under the Imperial Government of India considered post-war development and decided that self-sufficiency in the production of essential drugs was desirable. Penicillin, sulphonamides and antimalarials received top priority. In 1948 the new Government decided to establish a publicly-owned penicellin factory. A 200-acre site near the village of Pimpri, 10 miles from Poona, was selected and financial and technical help were provided by UNICEF and the WHO. In 1952 the foundation was laid and two years later most of the building had been completed. In June 1954 a joint stock company was registered in the name Hindustan Antibiotics (Pvte.) Ltd., the shares of which are vested in the President of India. Trial runs were made after December 1954, but it was not until March 1956 that regular production of penicillin started. The speed with which progress has since been made is illustrated by the following table of production:

	million mega units
1955-6	0·62
1956-7	9·9
1957-8	21·6
1958-9 (expected) ...	24·0

The product of the antibiotic company is packed in vials or bulk containers. Vialled material is handled by five distributing companies. Bulk penicillin is purchased by the companies operating in India who had previously imported it. The current home demand for penicillin in India is 50 million mega units and therefore even current production is capable of meeting only half of national requirements. A team of Russian experts who visited India in 1956 estimated that as medical facilities improve and the rural health programme gets under way penicillin requirements are likely to be doubled. A programme for expanding production facilities is in hand, and an increase in annual production of penicillin to 40 million mega units is expected by 1959-60. Hindustan Antibiotics prides itself on the quality of its product, all material passed for distribution conforms to the Pharmacopœia of the U.K., and of U.S.A.

Tuberculosis is an immense problem in India and not surprisingly the Government are anxious to establish a streptomycin plant as soon as possible. Current national requirements are estimated to be 45,000 kg. Hindustan Antibiotics hope to achieve this target within three years.

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The 1959 Corrosion Exhibition

Many exhibits for the chemical industry

The first Corrosion Exhibition organised by "Corrosion Technology" was held in October 1957 at the Royal Horticultural Society's Old Hall. This year's Exhibition is half as large again and will be held in the R.H.S. New Hall. There are over 100 stands, on which are being shown the latest methods of combating all types of corrosion problems. Here is a description of exhibits of special interest to manufacturing chemists.

The Place: Royal Horticultural Society's New Hall, Greycoat Street, Westminster, S.W.1.

Opening Days: Monday, Tuesday, Wednesday and Thursday, April 27-30.

Times of opening: Monday 11 a.m.-7 p.m. Tuesday and Wednesday 10 a.m.-7 p.m. Thursday 10 a.m.-4.30 p.m.

Readers of "Manufacturing Chemist" may obtain complimentary admission tickets on application to

The Organiser, Corrosion Exhibition, Leonard Hill House, Eden Street, N.W.1.

A.C. Plastic Industries Ltd.

Stand 105 (Balcony Hall)

This company is using rigid and laminated PVC, polythene, HD polythene, nylon and *Perspex* in a variety of applications, including fume extraction. The company has installed fume extraction plant complete with PVC fans and lip-extraction hoods from laminated PVC and PVC fume cupboards complete with ducting and polythene-coated axial fans. Pipe installations for conducting corrosive fluids are being made in polythene and PVC tubing.

Anglo-American Synco Corporation Ltd.

Stand 73

The main exhibit of these specialists in sprayed neoprene-based coatings, is a 30 in./24 in. centrifugal pump-casing which has been in operation for over 14,000 hr.

Other exhibits, including lined valves, pump impellers and scrubbing-tower trays, indicate the versatility of *Synco* neoprene linings which can be applied by the company's engineers to both new and ex-service equipment either in their works or on site.

Atlas Plating Works Ltd.

Stand 33

A general range of electro-plating is shown on the stand and includes decorative and protective finishes obtained by still-vat and barrel processes. Examples of work in various metals are shown, also Roto-finished parts and anodising, both by sulphuric and chromic acid. Tin nickel, which is rapidly establishing itself for protective and decorative finishes, is featured, as is brass plating on wire articles. The interesting development of plating plastic components is shown by specimen pieces. A specially equipped department offers depositions of hard chromium including plating direct on to aluminium. Precious metal deposits, with their high conductivity and anti-corrosive qualities, are also exhibited.

British Paints Ltd.

Stands 77/80

This stand will feature, by means of panels, specifications designed to deal with the following problems: internal corrosion in oil tankers, calorifiers, heat exchangers, steam boilers, economisers, etc., drinking-water tanks, crankcases of diesel engines, bridges and structural steelwork, external corrosion of ships' hulls above and below the water-line, and heavy-duty coatings for high abrasion, acid and alkali resistance. Also shown will be the priming of metal surfaces by means of various specialised coatings such as cold galvanising. The Industrial Finishes Division will be represented by examples of their stoving enamels, including hammer, wrinkle and polychromatic finishes and the new polyurethane coatings.

An interesting exhibit will show the behaviour of several coatings used in connection with cathodic protection. Another will illustrate what happens on the interior surface of a boiler tube while steam is being generated, together with the advantages to be gained by using the firm's *Apexior* process for such surfaces—even up to 1,000°F.

BTR Industries Ltd.

Stand 10

The results of many years' experience in anti-corrosion lining, covering and fabrication are indicated by the display of the BTR Group of Companies.

Exhibits will include: A range of rubber and ebonite compounds bonded to base metal. Demonstration circuit comprising an ebonite-lined pump, ebonite pipes, valves and fittings and a glass-fibre reinforced resin-bonded tank for corrosive applications. Moulded and fabricated ebonite components and corrosion-resistant vessels in gutta-percha. Industrial hose in textile reinforced rubber, P.V.C. and P.T.F.E. for service under corrosive conditions. A range of high-impact P.V.C. pipes and fittings including demonstration assemblies showing methods of jointings and degree of "set" obtainable in pipes for specific circuit designs. A selection of base metals coated with polythene, neoprene, hypalon, epoxy pitch, nylon and ceramic by flame spraying etc. Patent flexible P.V.C. jointing of acid-resisting bricks. Acid-resisting paints.

BX Plastics Ltd.

Stands 42/39

Chemical plant made from *Cobex* rigid vinyl and expanded metal laminates will be displayed with various exhibits of chemical plant equipment fabricated by leading manufacturers in this field.

Plant made from *Stelvetite*, the plastic-coated steel, will also be shown.

Cathodic Corrosion Control Ltd.

Stands 47/50

A new transistorised holiday detector, to be known as the *Perram Pacc*, is to be introduced. The detector, which will be demonstrated, is completely self-contained and has a resin-bonded fibreglass case. Light weight has been achieved by the use of a transistorised circuit, powered by six Varley dry accumulators.

A further feature of this new unit is that it operates on a D.C. output, enabling the equipment to be used with rolling springs regardless of the diameter sizes of the pipe to be tested and without interference due to pipe capacitance.

Cathodic Corrosion Control Ltd., from whom the *Perram Pacc* Holiday Detector is available for sale or hire, specialises in cathodic protection engineering by impressed current methods.

Cawley Plastics Ltd.

Stand 11

The main feature will be a dual laminate tank kept at boiling point for the period of the Exhibition. This method of constructing chemical storage and process tanks widens the number of uses of tanks in plastic materials and allows changes in temperature, shape and size previously thought to be impossible. The inner surface is unplasticised PVC and this is externally reinforced and bonded to polyester resin reinforced with glass-fibre.

A new fan in unplasticised PVC, which gives centrifugal fan performance in an axial flow type case, will be working on the stand.

Ciba (A.R.L.) Ltd.

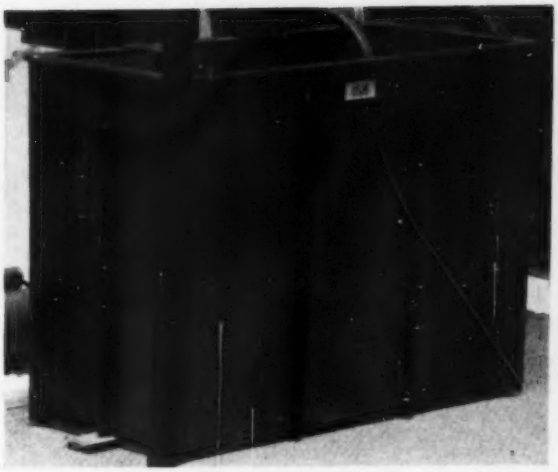
Stand 5/6

The Ciba (A.R.L.) Ltd. display will feature applications of the Araldite range of epoxy resins. These are used in the anti-corrosion field for protective paints, glass-fibre laminates, cements and stoppers, as well as for adhesives and potting compounds. The resins are said to cure without giving off volatile matter, and shrinkage is negligible. The resulting cured material is resistant to chemical and

atmospheric attack and has outstanding adhesion to many different materials including metals. The resins have strength, toughness and resilience and have good electrical properties.

The use of woven glass cloth impregnated with Araldite as a protective coating or raw material has been particularly successful. The resulting laminate has a high strength/weight ratio, is resistant to damage and is non-corrodible.

Electrical assemblies or components can be completely protected against atmospheric corrosion by potting or encapsulating them in Araldite.



Chemical tank of "Cobex" rigid vinyl made by BX Plastics Ltd. and laminated with expanded metal.

Corrosion Group, National Chemical Laboratory, D.S.I.R.

Stand 107 (Balcony)

The Group maintains a corrosion-abstract bibliography and advises on corrosion and related problems. Some typical problems will be shown together with the method of recording and classifying the data accumulated.

An illustrated description will be given of the type of water circulation system that is being used to investigate the corrosion of metal pipes by flowing water at various temperatures. The results should be of value in predicting the behaviour of metals in hot-water systems and in heat exchangers in general. A further objective is to develop inhibitors that will be effective at concentrations of 10 p.p.m. or less.

A preliminary research experiment will be shown revealing variation in the protection given by cyclohexylamine carbonate (CHC) to steel surfaces grossly contaminated with various salts and exposed to a humid atmosphere.

The mechanism of action of chromates as corrosion inhibitors in dilute aqueous solutions is being investigated using sodium chromate labelled with radioactive Cr^{51}. Adsorption of chromate on the surface of the metal and subsequent oxide film growth can be followed by measuring the amount and distribution of radioactivity. The equipment will be shown, together with some typical results.

Corrosion Ltd. and Coltrate Ltd.

Stand 108 (Balcony Hall)

Corrosion Ltd. will show examples of their long-established *Epiglo* and *Epi-tar* epoxy coating and of their new *Polytile* coating.

Coltrate Ltd. will demonstrate by photographs some of the many jobs they have undertaken for well-known companies. They are fully equipped with shot-blasting machinery, specialised application devices, and heat-curing equipment.

Corrosion Proof Products Ltd.

Stand 63

Corrosion Proof Products Ltd. are specialists in the anti-corrosive field and manufacture an extensive range of chemical-resistant cements, membranes and jointing compounds. The company's Contracts Department undertakes the laying of chemical-resistant tiled floors and drainage systems, and the construction of brick and/or membrane linings to storage tanks, acid towers and processing vessels, *etc.*

The company also has a Technical Department whose services are at the disposal of engineers, architects and consultants on matters relating to anti-corrosive specifications.

Samples are exhibited of the company's chemical-resistant cements and membranes which include: Furane resin cement; furane/phenolic resin cement; cashew nut shell resin cement; phenolic resin cement; epoxide resin cement; natural rubber latex cement; synthetic rubber latex cements; plasticised sulphur cement; silicate cements; polyester resin cement.

Du Pont Co. (United Kingdom Ltd.)

Stands 90/91

This company supplies neoprene, Hypalon and Viton synthetic rubber manufactured by E. I. du Pont de Nemours & Co. Inc. in the United States. It is anticipated that during 1960 the production of neoprene by Du Pont Co. (U.K.) Ltd. will commence at a plant at present under construction in Northern Ireland.

These elastomers are used in equipment for handling chemicals and oils where elastomeric properties are required, together with resistance to attack by the product being handled. Such items as tank linings, valve sleeves, gaskets, O rings, hoses and conveyor belts, are typical examples of this type of application.

In addition, these materials are utilised as the basic ingredient of high quality protective coatings used to prevent corrosion. Coatings made with them are weatherproof and are resistant to attack by many chemicals and oils as well as salt water. They may be designed for use at various temperatures and may be applied to several different types of surface including metal, concrete, masonry and wood.

This exhibit tells the story behind the use of Du Pont elastomers for corrosion-resistant service in both the types of application mentioned above. Typical examples of parts made with these materials and of coatings that may be used on various surfaces are shown, along with examples of their practical application in industry.

Ega Electric Ltd.

Stand 84

This company will exhibit non-metallic conduits, together with fittings and accessories. *Egatube* is made from unplasticised PVC and is impervious to most corrosive conditions.

Evode Ltd.

Stand 8

Evode Ltd., manufacturers of an extensive range of anti-corrosive and protective paints, are exhibiting the following items. Evokote Type 23. Epikote/pitch composition. This is a new addition to the range of Evokote paints. It is a two-part composition giving high film thickness per coat and showing excellent resistance to fresh and salt water, acids, alkalis, aqueous chemical solutions, oils, solvents and such combinations of these contaminants as are commonly met; for example, in plating shops, dyehouses, chemical factories, gas and electricity works, and marine and port installations.

Bitugel. First introduced at the 1957 Corrosion Exhibition, this is a heavy-duty bituminous anti-corrosive in gas works, coking plants, steelworks, and for piers and other marine installations, bridges and galvanized-iron roofs, etc.

Aluminium 308. Resists temperatures up to 1,000 F. and has good exterior durability. This material is suitable for the manifolds and exhausts of internal combustion engines, flues and the lower ends of chimney stacks, furnace doors, etc.

Evoled and Evodyne. These products have become established for protection of chemical plant and building structures subjected to highly corrosive conditions.

Evotect anti-bituminous paint. The necessity for sealing costs on bituminous-painted surfaces is eliminated by the use of this paint, thereby allowing the application of high-gloss colour to all such surfaces.

A. E. Griffiths (Smethwick) Ltd.

Stand 103 (Balcony)

A. E. Griffiths (Smethwick) Ltd. are exhibiting a range of their corrosion-resistant fabrications consisting of P.V.C. reinforced plastics and titanium heating coils.

On this stand are shown tanks suitable for electro-plating and processing operations. They are constructed in reinforced plastics, utilising both polyester resin and furane resin. Of special note is the tank built in accordance with their twin-shell

principle, utilising an inner layer of furane resin and an outer layer of polyester resin. For use with this tank is a titanium coil for the heating of the solution, which employs the latest developments in welded tube, as supplied by I.C.I.

The company are exhibiting a P.V.C. paddle-bladed-type exhausting fan with flanged inlet and discharge, capable of handling 1,500 c.f.m. and driven by direct coupled, totally enclosed 1½-h.p. motor. A fume scrubber unit shown is also made entirely of P.V.C.

F. Haworth (A.R.C.) Ltd.

Stand 96

The company are specialist contractors in anti-corrosion work and suppliers of materials to resist acid and alkali attack, for use by firms carrying out their own installations or repairs.

Examples of contracting work will be illustrated by large photographs and examples of built-up flooring. Applications of brick and tile linings for tanks, towers, etc., will be shown by models.

Samples of bricks and tiles used for concrete and metal protection, together with a full range of anti-corrosion cements produced by Haworths, will be shown to illustrate the work of the material supply service.

Imperial Chemical Industries Ltd.

Stand 67/68

This year I.C.I. Metals Division shows some of the many uses of titanium in chemical plant, and of titanium/platinum anodes for electrolytic cells and for cathodic protection.

Titanium has two outstanding properties—excellent resistance to corrosion and a high strength/weight ratio—the first of which is particularly recommended to the chemical industry for equipment handling many aggressive process liquors. A working exhibit shows how, by the use of an impressed positive potential, the corrosion resistance of titanium can be increased to cover an even wider range of aggressive media.

An economic non-consumable electrode for use in a wide range of electro-chemical processes is also featured. Exhibits show that by making a titanium electrode with a thin layer of platinum, which need not be continuous, a light robust electrode is produced. This will operate successfully in many media for long periods at very high anodic current densities without deterioration. Cathodic protection of a steel pier immersed in sea water illustrates one application of the new electrode.

The Metals Division of I.C.I. has many years' experience in the development of corrosion-resistant non-ferrous metals and alloys, such as copper, brass, bronze and aluminium, is now manufacturing titanium and zirconium on a commercial scale and undertaking considerable evaluation and development work on the " new " metals such as vanadium, niobium and beryllium.

Laminated Plastic Products Ltd.

Stand 14

This company, a new subsidiary of a well-known drug and fine-chemical house, specialises in the application of high-pressure asbestos-phenolic laminates to chemical plant.

One of the main exhibits will be the company's PTFE seated-ball-type plug cock, in pipeline form to show its advantages over the glass plug cock or weir type valve.

James Lithgow (U.K.) Ltd.

Stands 40/41

This exhibit will show what the firm can do and what it has done. Pieces of new plant and equipment coated with various *Calvinac* plastic coatings of both air dried and heat cured types will be shown. Items have been chosen from the soap, fine chemical, antibiotic, oil, salt degreasing, rayon, sugar, marine, biscuit and ventilation industries.

Loyne Ltd.

Stand 32

Loyne Ltd. specialise in applying surface coatings. On display will be a full range of samples and demonstration panels. Chemical resistant coatings included *Araldite*, *Epikote*, phenolics, neoprene, *Hypalon*, PTFE, polyesters and PVC. Anti-stick coatings include PTFE, silicones, metallisation, zinc, aluminium, linings, polyester, PVC and glass laminates.

The Donald Macpherson Group of Companies

Donald Macpherson & Co. Ltd.

Mody & Co. Ltd.

Stand 23

A comprehensive range of surface-coating systems will be shown suitable for combating all types of corrosive attack and examples will be exhibited of specific systems which have achieved practical success in a wide variety of fields, both industrial and marine. Among the industries covered are:

Chemical Industries, etc.: Here, a wide range of systems are shown suitable for applications in tanneries, dyeworks, acid manufacturing plants, soap and detergent factories, laundries, breweries, dairies, and various branches of the light and heavy chemical industry, including systems applicable to structural steelwork, sheet metal, non-ferrous metals, asbestos and concrete, etc.

The Gas Industry: Systems for gasholders, coke conveyor systems, retort houses, ammonia plant, purifier boxes, liquor tanks and structural steelwork.

The Oil Industry: Storage tanks, pipelines, various specialised plants in refineries, road tank wagons, marine tankers, steel structural work. *The Electricity Undertaking.* Transmission pylons, condensing systems, atomic energy and conventional generating station equipment. *Marine Installations and Shipping:* Various systems to resist weathering and sea-water attack are shown.

These systems embrace the most modern surface coatings based on recent developments, including epoxy resins, isocyanates, etc., and technical staff will be in attendance to advise on particular problems in any of the above fields, and to give recommendations as to pretreatments, surface preparation and the coating system advised.

Neuchatel Anti-Corrosion Ltd.

Stand 34

Models, specimens and photographs will demonstrate aspects of this company's range of anti-corrosion services, including: pipelines, glass-fibre reinforced bitumen and coal-tar enamel coatings; membranes —flexible, acid resisting and waterproof, asphalt, rubber and resinous types; brickwork and tiling; and tank linings and coatings of various synthetic rubber and plastic resin types.

The high voltage "holiday-detection" system of determining the efficiency of completed coatings will be demonstrated.

Nordac Ltd.

Stand 44

Rubber, lead and plastic-lined chemical equipment will be shown. A scale model of a hydrochloric acid storage installation will be on display, indicating the filling pipe, fume vent and a simple method of scrubbing the HCl fume which is discharged through the vent pipe.

Packaging Centre

Stand 104 (Balcony)

Many of the most important modern packaging techniques and a vast amount of specialised packaging and packing materials are expressly designed to eliminate or to limit the corrosion of goods in store and in transit.

The Packaging Centre's display will illustrate this theme. It is in effect a "trailer" for a full-scale feature exhibition on this subject, soon to be staged at the Centre. This special display—"Packaging versus Corrosion"—is being sponsored by *Corrosion Technology*, the leading journal devoted to anti-corrosion techniques and services. It will be designed to give immediate practical help to every industry faced with corrosion problems—with the active collaboration of *Corrosion Technology's* technical staff.

Plastic Constructions Ltd.

Stand 18

Exhibits will include a centrifugal fan made from high density polythene throughout; a centrifugal fan made from rigid PVC throughout; a PVC carboy pump; a PVC laboratory pump; a tank made from reinforced glass fibre material and lined internally with PVC; and an air agitation coil made from high density polythene.

Prodorite Ltd.

Stands 35/38

Prodorite Ltd. carry out complete installations, including the original design and construction on site. Their work covers chemical engineering and acid-proof constructions of tanks, floors, process vessels, drainage and effluent schemes, fume extractions, etc., embodying special cement mastics, synthetic-resin surface coatings and plastic fabrications in polythene, rigid PVC and *Orglas* resin/glass laminates.

St. Helens Cable & Rubber Co. Ltd.

Stands 25/26

This exhibit is representative of "9-Group Protection," under which are grouped the wide range of *Cabtyrit* compounds for protecting plant from corro-

Shell V.P.I. 260 powder prevents corrosion of these precision metal parts.

sion. These comprise natural rubber, heat-resisting natural rubber, abrasion-resisting natural rubber, ebonite (hard rubber), ebonite (low-temperature vulcanising), flexible ebonite, polychloroprene (neoprene), PVC, butyl and butadiene acrylonitrile rubber—a range able to provide a solution to most problems of chemical corrosion. Special compounds are developed where called for to meet individual requirements.

Shell Chemical Co. Ltd.
Stands 58/59/62

Shell Chemicals provide not only for the protection of corrodible materials, but also for the construction of equipment from non-corrodible plastics.

Epikote epoxy resins — condensation polymers of epichlorhydrin and diphenylolpropane—range from free-flowing liquids to high melting solids. Materials based on these resins are said to be tough, flexible, highly adhesive and resistant to a wide range of chemicals.

Carina PVC and *Carlona* polyethylene (Ziegler-type, high density polymer) will be shown. The Shell vapour phase inhibitor which represents a new technique in corrosion prevention, either in the form of crystals or impregnated paper, will also be on display.

Smith and Nephew Ltd.
Stand 57

The main feature of this stand is devoted to the application of Lasso P.V.C. protection tape. This tape is said to be particularly valuable for the protection of joints on pipelines carrying oil, gas and electric cables, above or below ground. The Lasso Lap-o-Pipe machine is demonstrated on the stand.

The Tin Research Institute
Stand 4

This exhibit will show the value of "block" tin coatings against corrosion of all kinds.

By " block " is meant a cast coating of pure tin obtained by dipping articles in molten tin. It is non-toxic and can therefore be used in contact with foods. Equally important, it endows any metal with perfect solderability. The Institute will show how industry uses this block tin finish for fire extinguisher bodies, water heaters, milk churns and many other articles.

Tretol Ltd.
Stands 87/88

The principal conditions for which the materials of this comprehensive display of protective-coating systems have been designed are: chemical (wet and dry); marine; radioactive; high temperature and atmospheric. The more important materials in the Tretol range include:

Tretol chlorinated rubber paints. These paints are said to have first-class resistance to acids, alkalis and wet conditions. They are suitable for practically all general-purpose protective painting where difficult atmospheric conditions occur, and also in marine and coastal environments. A special grade has been developed for use in radioactive areas.

*Tretol Chemiprufe Enamel M.*90. This one-pack modified epoxide enamel meets the need for a glossy decorative paint system which will provide maximum protection to steel work and machinery where corrosive chemical fumes are present.

Tretol cold-cured epoxide enamels. These two-pack coatings are recommended for use in conditions where contact with solvents or immersion in acids and salts would render unsuitable a conventional air-drying protective system.

Tretoprene 2C System. For the protection of metals and concrete against very heavy chemical attack. A two-coat application on primed surfaces is claimed to give a film build-up equivalent to a dozen or more coats of ordinary paint.

Tretol heat-resisting coatings. These include high-temperature aluminium paints, and H.R. black enamel, which is designed to give protection against sulphurous fumes and acid condensates.

Tretol Coal Tar/Epoxy 177. This two-pack system provides a tough, tenacious coating in two coats and is claimed to have outstanding resistance to chemical attack by immersion or splash.

The United Paint Co. Ltd.
Stand 54

The United Paint Co. Ltd. is exhibiting a comprehensive range of products. One item of interest is Visco-Led red-lead paint (B.S.S. 2523)—claimed by the manufacturers to be a unique product, which overcomes the problem of settlement and wastage frequently experienced with red- and white-lead paints. Included in this range will be Visco-Led epoxy red lead, a high-grade anti-corrosive primer, which has exceptional adhesion and resistance to acids and abrasion.

Among their other specialities is Clor-O-Cote, an acid-resisting paint for application by brush or spray, giving perfect protection against the action of acids, alkaline solutions and other corrosive forces.

Winn and Coales Ltd.
Stands 1/2

Although *Denso* tapes will always form the backbone of the *Denso* system, visitors to their stand will find the emphasis on the complete anti-corrosion service offered by Winn and Coales Ltd. of London. The non-oxidising and non-

Moulding Denso tape on to the contours of a pipeline joint

setting properties of petroleum jelly (the basis of the various *Denso* compounds) are changeless. However, with the growth in the use of plastics, it has been found practicable to laminate a film of PVC to *Denso* tape and *Densopol* now provides the advantages of *Denso* with a tough, dry exterior, giving increased mechanical strength and an even higher electrical resistance.

Simple, cold, on-site application enables *Denso* to be handled by inexperienced labour; at the same time, its correct use is imperative if lasting protection is to be achieved. With this in mind the Company has formed its own Contracting Department (centred on their northern area H.Q. at Sale) capable of undertaking any required application, but with its main objective the servicing of structural steelwork which calls for more specialised attention than does pipework or other, easily wrapped surfaces.

Another example of *Denso* expansion in post-war years is the complete Cathodic Protection service, from initial survey to regular maintenance.

Yorkshire Imperial Metals Ltd.
Stand 93

" Yorkshire Imperial " service includes research, investigation and prior installation work to determine the correct alloy to meet individual service requirements.

Amongst the products to be displayed are: " Yorkshire Imperial " solid drawn tubes in copper and a wide range of special copper-base alloys such as the well-known *Yorcalbro/Alumbro* (aluminium-brass), *Yorkshire* 70/30 *Cupro-Nickel/Kunifer* 30. *Yorcoron/Kunifer* 30*A*, *Yorcunife/Kunifer* 5 (copper-nickel-iron), *Yorcunic/Kunifer* 10," etc.

Bi-metal tubes and bi-metal plates for conferring resistance on both sides to dual corrosion conditions, especially in heat exchange equipment in the oil industry.

Kuterlex PVC and polythene covered copper tubes for gas and water service pipelines installed in aggressive surroundings.

Plastics tubes and fittings including polythene, *Plastronga* and high impact PVC.

Copper and *Yorcasal* non-dezincable tube fittings.

BOOK REVIEWS

The Analytical Uses of Ethylenediamine Tetraacetic Acid

By Frank J. Welcher. Van Nostrand. Pp. xvii+366.

THE publishers' note on this book states that "the significant work done on the application of EDTA and its salts in analysis and control, appearing in the world-wide literature up to this time, has been detailed in this important volume."

The reviewer's opinion is that it has done just that. In general, anyone investigating a particular problem will need to go back to the original papers, so that this work can be considered as a compilation of notes and references.

There is no attempt to be selective, to state whether or not procedures for analysis have been checked in other laboratories or whether or not they are recommended by the author. The question of whether the time that could be saved by using this book instead of indices of abstracts justifies its inclusion in a library depends on the outlook of the librarian and his associates, but surely it would have been much more useful to laboratory chemists in general to have published a few selected, well-tried and established analytical methods rather than this compendium of 963 references.

J. H. MARTIN.

Ion Exchangers in Organic and Biochemistry

Edited by C. Calmon and T. R. E. Kressman. Interscience. Pp. 761. $15 *net.*

THIS monumental compilation on ion exchange consists of contributions by specialists in various aspects of the subject which have been edited by two scientists employed respectively by the Permutit Co. in the U.S. and the Permutit Co. in Britain.

The book consists of three parts: The first two deal with the fundamentals of ion exchange and the techniques and apparatus used and the third part with its application to organic and biochemistry. Both the ion exchange properties of biochemical systems as well as the applications of conventional ion exchange materials to biochemistry and to organic chemistry are dealt with. Aspects of the subject considered in the third chapter include the ion exchange characteristics of body tissues and cells, organisms, protein materials, special body products and fluids, pharmaceutical and medical applications, plants and plant products, foods, organic chemistry and water.

The book is undoubtedly comprehensive and authoritative. Its comprehensiveness, however, may not appeal to the reader interested in only certain aspects of the subject and who will, therefore, begrudge paying for information he does not want.

Bookshop Service

All books reviewed in MANUFACTURING CHEMIST and all other scientific or technical books may be obtained from: Technical Books, 308 Euston Road, London, N.W.1. Telephone: Euston 5911.

Pharmacology of Plant Phenolics

Edited by J. W. Fairbairn. Academic Press, London, 1959. *Pp.* 151. 30*s. net.*

THIS book is of a type which has become common in the biological field, representing as it does the proceedings of a symposium held at Oxford in April 1958 by the Plant Phenolics Group. Eleven papers presented at the symposium are placed on record together with numerous references and an edited note on the discussions which followed each paper. In some cases the discussions are almost as valuable and stimulating as the papers themselves.

The scope of the work, though confined to non-nitrogenous compounds, is somewhat wider than might appear from its title. Thus while the material is of prime interest to workers in the field of plant phenolics, there is much which will appeal to chemists and biochemists who have a leaning towards pharmacology. This is particularly true of the contributions by Professors J. H. Burn and R. T. Williams respectively. Professor Burn's introductory paper does not in the strict sense deal with plant phenolics at all, being in fact a lucid and non-technical account of the present state of knowledge on the functions and modes of action of adrenaline, noradrenaline and 5-hydroxytryptamine. Opportunity might have been taken to mention that noradrenaline and 5-hydroxytryptamine have now been identified in certain plant tissues, notably in bananas. In Professor Williams' up-to-date account of the metabolism of phenols in man and laboratory animals the accent is on the mechanisms underlying the urinary excretion of phenols in general rather than of plant phenolics in particular. Papers by W. B. Whalley, J. W. Fairbairn and J. D. Biggers cover such topics as the toxicity, cathartic, œstrogenic and photodynamic actions of plant phenolics. Various aspects of the influence of flavonoids on capillary permeability are dealt with by Miss M. F. Lockett, F. DeEds, J. Lavollay and J. Neumann. The book is completed by a very useful and readable account by E. C. Bate-Smith of the distribution of phenols in the most important families of edible plants.

The standard of production is the high one normally associated with this publisher. The numerous chemical formulæ are clearly presented with the exception of those on page 33 in which the carbonyl groups have been printed as cobalt atoms. There are a few minor misprints, the most remarkable being on page 87, where "blackcurrants" is rendered as "black currents." The statement on page 31 that the antihæmorrhagic action of dicoumarol is due to a reduction in the prothrombin content of the blood is inaccurate, it being now well-established that dicoumarol acts on several blood coagulation factors, notably Factor VII and Christmas Factor. While the provision of an index would have been an improvement, the omission may be due to a desire to minimise the inevitable delay in publication.

D. M. SHEPHERD.

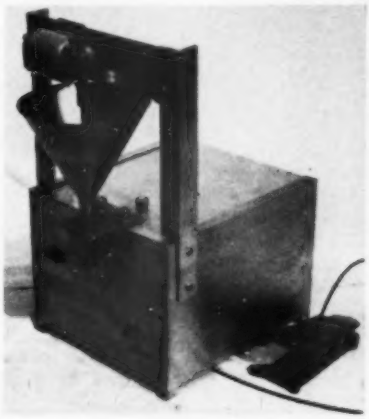
PLANT AND EQUIPMENT

▶STERILE FILLING FOR SEMI-SOLIDS

A. J. Manning Ltd. manufacture the *Model* 48 motorised filling machine for filling comparatively small quantities of semi-solids and very viscous solutions under sterile conditions. The machine incorporates a stainless steel glandless measuring pump with mechanically operated valves. The supply hopper is mounted on the measuring pump and the whole sterilisable unit is clamped in position by means of two thumb nuts. A fine micrometer adjustment to the radius link and quadrant movement is used for pump output adjustment, and this is said to be both accurate and infinitely variable. A single cycle clutch is incorporated and the machine is set in operation by means of either hand or foot control. A standard speed range of 10, 15, 20, 25 cycles per min. is obtained through a cone pulley and vee belt drive from a ¼ h.p. motor. Other speeds can be arranged to suit special requirements.

A range of measuring pumps 0·5 ml. to 5 ml., 1 ml. to 10 ml., 5 ml. to 30 ml., and 10 ml. to 50 ml., can be supplied with the machine, and larger sizes can be built to special order. Various types and sizes of plain or jacketed hoppers can be supplied to suit users' requirements. Special attachments available include a stirrer or impeller and a six-figure counter.

The filler is 16 in. wide by 24 in. deep by 30 in. high and weighs 150 lb.



The *Model 48* motorised filler for semi-solids. A variety of plain or jacketed hoppers is available.

▶UNIVERSAL MIXER

The *Universal* mixer, made by Premier Colloid Mills Ltd., is said to combine the advantage of a permanent installation with the versatility of a portable mixer. Finished in stove enamel, the mixer has a stainless steel shaft which is available in several lengths, and which is said to take only a short time to change from one length to another. A stainless steel marine-type propeller matches the particular speed and horsepower of the unit recommended, or a Premier *Dispersator* may be used instead. The basic unit comes in 25 variations of power and speed and, it is claimed, can mix batches up to 500 gal.

Totally enclosed or flame-proof, the motors are available from ¾ h.p. to 2½ h.p., with speeds from 700 to 3,000 r.p.m. in addition to motors with two speeds for handling products of varying viscosities. A handle makes the mixer relatively easy to transport, and there is a double clamp to cope with heavy work.

This *Universal* mixer is available in 25 different combinations of power and speed.

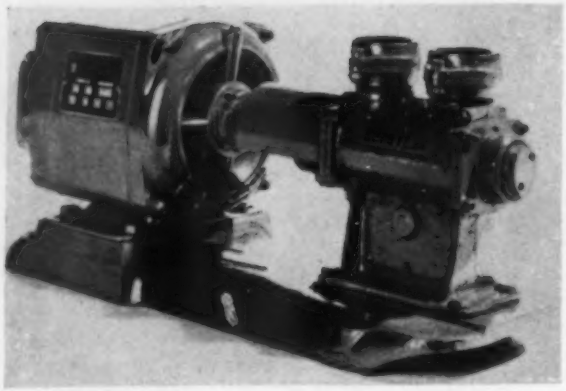
▶FILTER PRESSES

Durham Raw Materials Ltd. have been appointed sole selling agents in U.K. for the filter presses manufactured by F. H. Schule Ltd., Hamburg. The presses can be supplied to standard patterns, or tailor made, to cover any industrial filtration application, particularly in the chemical, paint and varnish, drug, food, oil, textile and mining industries. The presses are of two basic types: flush plate and frame presses, for use where the filter cake is of uniform thickness and porosity, and facilitates an effective flushing of the solids; recessed plate presses, for use where solids are subject to blockage. Both these types of press are available with plate sizes from 9¾ in. to 57 in.

Filter presses, bodies, plates and frames are manufactured in the materials most suitable for the intended application. Those most commonly used are close-grained cast iron, high-quality steel and steel alloys, stainless steel, aluminium, copper, bronze, hard rubber and suitable woods. To resist corrosion or abrasion, filter plates and frames may be covered with protective coatings. Other special features which can be incorporated include: channels for circulation of steam or cooling agents, gas-proof filter elements, and plates and frames for high filter pressures.

A light-weight filter press is available for applications for which a maximum pressure of 45 lb. p.s.i. is stipulated. These presses are manufactured in standard profiles, from light-weight materials. A light-weight plate is also supplied. This is said to permit easier handling and better filtrate discharge and to cause less wear and tear of the filter cloths. A special laboratory filter press with a 5 in. plate, fitted with *plexiglass* frames and plates, is available to provide for visual control of the filtering and washing processes.

The presses are supplied with either mechanical or hydraulic closing devices. The latter incorporate the Schule hydraulic spindle which is claimed to make this form of closure possible without the use of pumps, valves, pipes and liquid containers.



Right: Quick-action pipe coupling available from Simon Handling Engineers.

Left: The Goodyear process pump. This is self-priming and delivers 5 g.p.m. at 1,440 r.p.m.

▶QUICK-ACTION PIPE COUPLING

A quick-action pipe coupling for pneumatic or hydraulic pipelines has been developed by Simon Handling Engineers Ltd., said to be capable of withstanding considerable pressures, and to be equally suitable for use on rigid or flexible pipes, the coupling uses lever and claw fastenings to make or break connections, while a fitted rubber sealing ring gives an airtight connection.

Each coupling consists of two rings with flanged ends. Fixed to one ring are the spring-loaded claw fasteners. A connection is made when the two flanges are united and the claws closed over the joint so that the flanges are held tightly together, forming an air-tight seal. Couplings are made for welding on to 2 in.-8 in. thin-walled rigid or flexible pipes and for screwing on to heavier pipes.

▶PROCESS PUMPING SET

A compact light-weight pumping unit is available from Goodyear Pumps Ltd. It is specially designed for food and chemical processing applications, factory and laboratory installations, and it is also said to be suitable for general pumping duties.

To a Goodyear *Size A5* positive displacement pump is coupled a Newman *Elf* ¾ h.p. AC electric motor mounted on a light-weight aluminium bedplate casting. The pump, with a normal operating speed of 1,440 r.p.m. delivers 5 g.p.m. According to the manufacturers it is self-priming and can run with a dry suction for long periods, making it suitable for emptying vats and barrels completely. They also claim that the pumping unit is capable of handling viscous fluids and fluids which contain suspended solids.

The rubber-to-metal type pump has only two moving parts in contact with the liquid, the plate wheel and rotor. The taper roller bearings are grease packed, and radial face shaft seals are fitted. A special feature claimed for the design is the cast light alloy bedplate, curved over its central span for rigidity and ease of cleaning. Provision is made for two lifting handles, one on each side of the unit, using the same bolt holes as for the permanent installations. The pump is driven through a Spencer Moulton *Jubo* coupling protected by a metal guard. It is stated that this pump set is virtually silent when running on full load and it can be commended for duties where quiet running is an important consideration.

The set with *Mechanite* pump weighs 46 lb. Dimensions are 20½ in. long, 7¼ in. wide and 9½ in. high. The set can also be supplied with pumps in bronze, light alloy or stainless steel.

▶CONTAINER FOR LIQUID NITROGEN

A 25 litre cryogenic container for the transport and storage of liquid nitrogen is available from the Linde Department of the Union Carbide International Co.

Named the *LC*-25, the container has been designed for use in dermatology as well as for service in hospitals, clinics and medical research laboratories. It weighs 19 lb. empty and has a large neck opening stated to make it suitable for use as a refrigerator for freezing and preserving small biological specimens under 1½ in. dia. Constructed entirely of welded aluminium, the container consists basically of two concentric shells with the space between the shell walls drawn to a vacuum and filled with an insulating material to minimise evaporation loss. It is 15⅜ in. in diameter by 22¾ in. high and is fitted with a shock-absorbing base. Evaporation loss per day is said to be 5% max.

▶GRANULATING AND MILLING

In the *Rotorgran* oscillating granulator, a rotor, which consists of bars arranged cylindrically, oscillates over a woven wire mesh screen and forces material through it. The screens are interchangeable and determine the particle size of the final product. A hopper is arranged above the rotor and the material drops by gravity through the spaces between the bars of the rotor. The hopper, rotor and all other parts in contact with the material to be reduced are of stainless steel.

The manufacturers, Manesty Machines Ltd., say that the machine can be used to reduce both wet and dry materials.

The same company also make a drug mill suitable for reducing dry, crystalline and granular products. It is of the cone type, in which an inner cone revolves at about 300 r.p.m. within a fixed one. The distance between the two cones, which determines the size of the product, can be adjusted by a thumbscrew. In operation, material is fed from a hopper above into the space between the two cone faces. A breaker bar, which rotates with the inner cone, projects upwards into the hopper and assists feeding.

For more information about the plant and equipment described please use the coupon on page 184

NEWS . . .

Commons debate drug prices

N.H.S. efficiency council appointed

Opening a debate in the House of Commons on March 12 on a supplementary vote of £16,589,706 for the National Health Service, the Minister of Health, Mr. Walker Smith, said that there were two reasons for the increase—the general upward trend of costs and the introduction of new drugs. For example, antibiotics and a cardiac preparation accounted for 40% of the total increased costs of prescriptions.

The cost of these new drugs, he continued, must be balanced against their value to the community not only medically but also for the contribution they made indirectly to the national economy by shortening illness and permitting a speedier return to work.

Dr. Edith Summerskill said that the shilling prescription "tax on the sick" had resulted in the nation's drug bill soaring. When it was imposed in 1956 the cost of a prescription was 4s. 6d. Today it was 6s. 5½d. Would they now abolish the charge to reduce over-prescribing? Prices for corticosteroids had dropped from £56 to £12 for 1,000 tablets during the four months from July, 1958. This price reduction was by stages, which were all followed by the leading American-owned or American-licensed companies in the U.K.

Mr. Maurice Edelman said that the responsibility for the substantially increased costs, particularly for proprietary medicines, lay in the fact that those drugs had fallen into the hands of a ring of producers which was in effect demanding of the consuming public prices which, if they were translated in terms of other products, would cause tremendous protests all over the country.

He believed that there was today a two-fold process going on. On the one hand there were the scientists working for science; the second, and socially immoral stage, was when these developments and discoveries were taken up by commercial companies and not used simply, directly and primarily to make them available for all the people, but to reinforce the price ring which was used to exploit the sick.

Speaking on the cost of poliomyelitis vaccines Mr. Richard Thompson, Parliamentary Secretary, Ministry of Health, said that the price paid for British vaccines was substantially higher than the price recently paid for American or Canadian vaccine. Vaccine had not been purchased from all the American manufacturers, and identical quotations were not received from those from whom they did buy. Prices quoted by British manufacturers were not uniform.

Maximum importance was attached to getting the best possible value for money in the Health Service. A council had been set up to assist in the development of efficiency techniques with Sir Ewart Smith (a director of I.C.I.) as chairman. The Minister was also studying the first report of the firm of management consultants which had undertaken a study of the operations of four representative hospitals.

Last dinner of Chemists Federation

"The Chemists Federation is dead; long live the principles of the Chemists Federation." This was the sentiment of a dinner held in London on March 24 at which the council of the Federation entertained officers of other pharmaceutical organisations and others who had assisted them in the recent action before the Restrictive Practices Court which resulted in a verdict which compelled the winding-up of the Federation.

The President of the Pharmaceutical Society, Mr. D. W. Hudson said the death of the Federation was a public calamity. The principle for which it stood—the restriction of the sale of medicines and drugs to chemist shops—was clearly of benefit to the public. It was quite wrong that medicines should be sold in the same way as bottles of sauce or packets of soap powder and he had no doubt that it was not the intention of the Act that the safeguards inherent in the CF method of distribution should be jettisoned.

These views were echoed by the other speakers—Capt. R. C. Kelly, chairman of the Crookes Laboratories Ltd., Mr. F. E. Mellor, immediate past-president of the CF, Mr. Harold G. Moss, chairman of the National Pharmaceutical Union, and Mr. S. J. Stearn, the senior past-president of the CF present at the dinner.

During the dinner miniature badges of office were presented to ten CF past-presidents, the immediate past vice-president, and to the immediate past-treasurer. The presentations were made by Capt. Kelly, whose firm had presented to the Federation the badge and chain of office worn by the successive presidents. Finally this chain of office was presented to Mr. Moss for permanent display in the headquarters of the National Pharmaceutical Union in London.

Thus closed the last chapter in the history of the CF but the mood of the gathering was clearly that the organisation had been unjustly condemned and that the principle of distribution of medicines through chemists should have been upheld.

Ward Casson buy factory

Ward Casson Ltd., have started a programme for the development and production of new pharmaceuticals. They have acquired a factory at 2 Bardolph Rd., Richmond, Surrey, which is now being re-equipped. It is under the technical direction of Dr. D. O. Holland, who joined Ward Casson last November. Before then he was assistant director of research of Beecham Research Laboratories Ltd., where he was in charge of the research work which culminated in the isolation of penicillanic acid (see p. 143).

Ward Casson are a new company in pharmaceutical manufacturing, although they have been established for many years as traders. The directors are J. M. Goldsmith, E. R. D. Goldsmith and J. W. Snow, M.P.

All correspondence should be addressed to the Richmond premises, Telephone Richmond 6425.

British Cellophane form new Division

British Cellophane Ltd. has formed a Plastic Films Division for the manufacture and marketing of films other than *Cellophane*.

Mr. J. Schwartz, who has been with the company since its formation in 1935, and was recently sales service manager, has been appointed manager of the new division. Production manager is Mr. D. Noble, and the sales manager is Mr. D. F. H. Drew.

The Plastic Films Division is at present producing and marketing BCL polythene film and is also developing *Lubrithene* (a multi-ply thermoplastic material used as a separating membrane is concrete-laying) which BCL introduced in 1958. In addition, the Division is marketing three other films; Dupont's *Mylar* (polyester) film, the unplasticised PVC film manufactured by La Cellophane S.A. of France, and the bi-axially orientated polystyrene film made by B.X. Plastics Ltd.

Mixing machine company plans for expansion

Peerless and Ericsson Ltd., manufacturers of industrial mixers and food machinery, have been acquired by the Kenwood Manufacturing Co. Ltd. At a press reception held in London last month, Mr. Kenneth Wood, chairman of Kenwood, emphasised that the high standards of Peerless and Ericsson machines would be maintained and improved. The design of these machines was excellent, he said, and it was hoped that the combination of the two firms would lead to further improvements. Servicing and supply arrangements would continue and owners of Peerless and Ericsson machines could be assured that their requirements would be fully met.

Production is centred at the works at King's Norton near Birmingham. It is now in the process of expanding its output.

Sales office opened

Kingsley and Keith Ltd. have opened a Northern sales office at 10 Manchester Road, Bury, Lancs., Telephone: Bury 2747. The manager is Mr. J. A. Wright.

Radiochemical centre reorganised

Production and marketing of radioactive isotopes, until now shared between the Radiochemical Centre at Amersham and the Isotope Division of A.E.R.E. at Harwell, has been centralised into a single comprehensive organisation for producing and marketing all such isotopes.

Dr. W. P. Grove has been appointed Director of the reorganised Centre, which has its headquarters and principal laboratories at Amersham and will have irradiation facilities at Harwell and at other Authority sites.

The reorganisation is already effective, but users of radioisotopes should continue, until they are advised of new arrangements, to order their requirements from Amersham or Harwell as they have done in the past. Research into the properties of isotopes and new applications of them and their radiations will be continued by an Isotope Research Division at Harwell and at the Wantage Radiation Laboratories. This division will continue to operate the Isotope School.

Both the Radiochemical Centre and the Isotope Research Division will remain part of the Research Group of the Atomic Energy Authority.

New D.S.I.R. laboratory to open in June

The Lord President of the Council (Lord Hailsham) will open the new Warren Spring Laboratory, D.S.I.R., at Stevenage, on Monday, June 29. The laboratory is intended to assist Government departments and industry by resources that are not available in any other establishment of the Department, and will carry out research and development in a wide field and will not be limited to particular aspects of technology. Its initial programme will include work on mineral processing, the synthesis of oils and chemicals from carbon monoxide and hydrogen, and research aimed at the suppression of atmospheric pollution. Much of this work will be of a chemical engineering character and will require basic chemical engineering research to be undertaken in parallel with it. The station will be free to take up any research requiring staff and facilities of the type that are being provided.

For the time being, research on atmospheric pollution will continue at Greenwich, where the address is: The Atmospheric Pollution Division, Warren Spring Laboratory, River Way, East Greenwich, London, S.E. 10.

Technical Press Review—April

Chemical and Process Engineering.—New Applications of Plastics in Chemical Plant; Graphite as a Material of Construction for Heat Exchangers; Meehanite as a Material of Construction for Chemical Plant; Pumping Developments; Preview of Engineering, Marine, Welding and Nuclear Energy Exhibition.

Corrosion Technology.— Preview of the 1959 Corosion Exhibition; Corrosion Research in the U.S.S.R.

Automation Progress.—Cost Accounting in Conditions of Automation; Technological Progress in the Glass Industry; Electronic Process Control—Scope and Advantage; Transient Response in Electromagnetic Clutches; Can We Build a Self-optimising Plant?; The Present State of Digital Technique.

Petroleum.— Utilisation of Residual Fuel Oil—3; Corrosion Problems With Pressure Vessels; China's Growing Oil Industry; Aspects of Refinery Corrosion Due to Crude.

Atomic World. — Uranium Dioxide as a Reactor Fuel; Metallic Uranium—Today's Reactor Fuel; Nuclear Fuel Cycling.

Paint Manufacture. — How Paints Stand Up to Tropical Climates—2; Lead in Corrosion-resistant Paints—Experiences in Britain and Sweden; Hazards in Paint Factories.

Food Manufacture. — Fumigation With Ethylene Oxide; Insects and Stored Foods; Experiments in Cooking Sardines—1; Food Production in Russia; Sugar Production in the Dominican Republic; Annual Review—Brewing.

Dairy Engineering.—Natural and Artificial Causes of Radioactivity in Milk; Cleaning and Maintenance of Walls and Floors in the Dairy; Bulk Handling Progress in Scotland; Selling Milk to Two Nations.

World Crops.—The Profitable Use of Fertilisers; Basic Factors in Herbage Production; Potassium for Pastures; The Importance of Silage; Fighting the Cocoa Capsid in Ghana—2.

For specimen copies and subscription forms apply to the Circulation Manager, Leonard Hill House, Eden Street, London, N.W.1.

Laboratory equipment shown

Quickfit and Quartz Ltd. gave a special exhibition of laboratory apparatus for teaching purposes at the South-west Essex Technical College and School of Art, Walthamstow, during the College's "Open Day" last month.

Diversey plans for U.K. operations

Mr. Albert Gale has resigned as director and secretary of Milton Antiseptic Ltd., to become managing director of Diversey (U.K.) Ltd., and Deosan Ltd.

This follows the recent acquisition of Diosan by Diversey (U.K.)—not by the parent company, Diversey Corporation, as stated in our February issue. Deosan was formerly one of the Milton Group of companies which has now been bought up by the Vick Chemical Co. of America through its British subsidiary, Vick International Ltd.

The issued share capital of Diversey (U.K.) Ltd. is £300,000. The Diversey Corporation encourages the participation of local capital in its activities.

While Diversey (U.K.) will receive some direction from the Diversey Corporation, it is possible that with successful development during the course of the next financial period the English company may place its shares on the market.

Diversey (U.K.) are the owners of the factory at Riddings, Derbyshire, where Deosan products are manufactured, and it is intended that Diversey products will also be made at the Riddings factory.

Diversey (U.K.) will be the manufacturing unit, while Deosan will continue as the selling organisation.

There will be a considerable increase in production of the company's products, which consist of sterilisers, detergents and fine chemicals. The company does not manufacture fertilisers.

The Diversey group of companies operate 21 factories. There are eight factories in the U.S.A., including an electronic, mining and a special alkane sulphonation unit which is in the Chicago factory. There are three factories in Canada, including one in Newfoundland, and a unit for the manufacture of a special chlorine containing sodium phosphate.

One factory is in Puerto Rica and includes in its production the preparation of sodium hypochlorite. One factory is in Venezuela. Two factories are in Brazil, including one for the production of phosphoric acid and a unit for the sulphonation of alkane as well as for the production of soap. There is one factory in Australia. Two factories are located in Hawaii, including one which produces agricultural insecticides.

The factory in England includes the manufacture of sodium hypochlorite in its products.

There are two factories in France.

The chairman of Diversey (U.K.) is M. M. Mackenzie. Other directors are E. J. Tucker, F.C.I.S., and H. W. Kochs and J. R. Swihart (both U.S. citizens).

People

K. D. Williamson

K. H. Harper

S. M. Peretz

E. Le Q. Herbert

H. S. Hibbins

W. Johnston

George Emerson, M.A.(CANTAB.), has joined A. G. Hersom as chief chemist. Mr. Emerson spent several years with Bourjois Ltd. at Reading and Croydon, and before this was with Morny Ltd. of Greenford.

E. W. M. Fawcett, technical director, and **H. P. P. Hodgkins,** commercial director of Howards of Ilford Ltd., have been appointed to the board of the parent company, Howards and Sons Ltd.

The board of Petrochemicals Ltd. have accepted the resignation of **W. E. Huggett,** who has been General manager of their Carrington works since 1955, when Petrochemicals Ltd. became an associate of Shell Chemical Co. Ltd. He has accepted an appointment with Constructors John Brown Ltd.

The new general manager at Carrington is **Dr. J. A. Berriman,** who joined Shell as a technologist in 1940, after completing his studies at Cambridge University. Since then he has had experience in Shell refineries, both in this country and in the United States. In July 1955 Dr. Berriman was appointed Director (Refining Division) and deputy to the managing director of Shell Refining Co. which position he has held until his present appointment.

Blaw Knox Chemical Engineering Co., Ltd. have appointed **Mr. Alan Sanderson,** A.M.I.MECH.E., A.M.I.GAS E., as sales manger. Mr. Sanderson's experience in the heavy engineering and process plant industries has been gained during his employment with plant suppliers, consultants and process operators.

E. A. Flack, late of W. J. Bush and Co. Ltd., has now joined Jacobson Van Den Berg and Co. (UK) Ltd., as sales manager—compounds and essences. He will control the sales of the products manufactured by their principals, Esrolko Ltd. of Dubendorf, Zurich, and Grindstedvaerket of Aarhus, Denmark, to the soft drinks, confectionery, flavour and perfumery industries.

V. Walters B.PHARM., F.P.S., has been awarded the degree of Doctor of Philosophy in the University of London for a thesis entitled "Studies on Bacterial Populations in Solutions of Phenols." Dr. Walters studied under **Dr. H. S. Bean** at Chelsea School of Pharmacy, where he was a member of the staff. He was recently appointed senior lecturer in pharmaceutics at the Nigerian College of Technology, Ibadan.

William Johnston, formerly with Imperial Chemical Industries Ltd., has been appointed a Director of Trans-Chemicals Ltd., a member of the Commercial Plastics Group of companies, 75 Grosvenor Street, London, W.1 (Telephone: HYDe Park 9261). Trans-Chemicals will buy the major raw materials for the Group, and buy on behalf of Paz Chemicals Ltd. (formerly Shell Chemicals Distributing Co. (Middle East) Ltd.)

E. Le Q. Herbert has been elected President of the Royal Institute of Chemistry for 1959-61. Mr. Herbert, who is managing director of Shell Refining Co. Ltd. and a director of Shell Chemical Co. Ltd., Trimpell Ltd., and Associated Ethyl Co., Ltd., joined the Shell Group in 1927 as a plant chemist. He served for nearly 12 years in Mexico before returning to the U.K. in 1938 and was appointed to his present position in July 1955.

Mr. Herbert is also a Fellow and Vice-President of the Institute of Petroleum, a Member of the Institution of Chemical Engineers and the Institute of Fuel, an Honorary Fellow of the Heriot-Watt College and a Governor of the Battersea College of Technology.

Obituary

Mr. R. R. Webster, an engineer with the A.P.V. Co., died on March 2 at the age of 62. He had been with the company for 26 years and for the greater part of this period represented them in the chemical, oil and varnish and distillation industries.

Changes in Boots' top management

Mr. H. S. Hibbins, vice-chairman of Boots Pure Drug Co. Ltd., is one of four senior officials of the company who retired on March 31. The others are Mr. S. Harker-Smith, Director of Merchandising, Mr. J. W. Seekings, manager of the wholesale and international divisions and a member of the company's executive committee, and Mr. A. H. Cragg, manager of the printing department.

The following appointments to the Board of Directors of the parent company took effect on April 1.

Mr. R. M. Dickson, who for the past seven years has been local director for the company in Scotland and since 1948 a member of the executive committee of management and a director of Boots Cash Chemists (Northern) Ltd.

Mr. K. H. Harper, who was appointed production manager of pharmaceuticals in 1954, came to the board of Boots Cash Chemists (Eastern) Ltd. in 1953 and was appointed a member of the Executive Committee in 1955.

Mr. K. D. Williamson, who joined the company in 1930, was appointed head buyer in 1955 and at the same time became a member of the executive committee of management and a director of Boots Cash Chemists (Western) Ltd.

The following appointments to the company's executive committee of management also took effect on April 1.

Mr. S. M. Peretz, who takes over management of the wholesale and international divisions, joined the company as an apprentice in Guernsey in 1933 and qualified as a pharmacist in 1940. In 1948 he was appointed publicity manager and in 1952 he became a director of Boots Cash Chemists (Southern) Ltd. In 1955 he moved to the wholesale and international divisions, where he has made a concentrated and detailed study of the company's overseas business.

Mr. A. D. Spencer is appointed a director of Boots Cash Chemists (Eastern) Ltd.

An additional appointment is that of Mr. A. P. Woodward, who becomes manager of the printing department.

More approved names for drugs

The British Pharmacopœia Commission has issued a further list of approved names, and the intention is that if any of the drugs to which these Approved Names are applied should eventually be described in the British Pharmacopœia the Approved Name should be its official title.

In some instances the names, other than the chemical names, appearing in the second column, are applied to preparations of the substance; they also include some registered trade marks.

Approved Name	Other Names
AZAPETINE	
1-Allyl-2 : 7-dihydro-3 : 4-5 : 6-dibenzazepine	Ilidar is the phosphate
CALCIUM BENZAMIDOSALICYLATE	
Calcium 4-benzamido-2-hydroxybenzoate	Aminacyl B-PAS; Therapas
DEXAMETHASONE	
9α-Fluoro-11β : 21-trihydroxy-16α-methylpregnal-1 : 4-diene-3 : 20-dione	Decadron; Deronil; Dexacortisyl is the 21-acetate
9α-Fluoro-16α-methylprednisolone	
DIMENOXADOLE	
2-Dimethylaminoethyl α-ethoxy-αα-diphenylacetate	Ditophal
DITOPHAL	
Diethyo dithiol*iso*phthalate	Etisul
FLUOPROMAZINE	
10-(3-Dimethylaminopropyl)-2-trifluoromethyl-phenothiazine	Vespral is the hydrochloride; Vesprin is the hydrochloride
HYDROCHLOROTHIAZIDE	
6-Chloro-3 : 4-dihydro-7-sulphamoylbenzo-1 : 2 : 4-thiadiazine 1 : 1-dioxide	Esidrex; Hydro-Saluric
HYDROFLUMETHIAZIDE	
3 : 4-Dihydro-7-sulphamoyl-6-trifluoromethylbenzo-1 : 2 : 4-thiadiazine 1 : 1-dioxide	Hydrenox; Naclex; Rontyl
MEBHYDROLIN	
5-Benzyl-1 : 2 : 3 : 4-tetrahydro-2-methylpyrid-(4, 3-*b*) indole	Incidal is the naphthalene-1 : 5-disulphonate
METHYLCHROMONE	
3-Methylchromone	Crodimyl
NORCODEINE	
N-Demethyl codeine	
NORMORPHINE	
N-Demethyl morphine	
ORPHENADRINE	
2-Dimethylaminoethyl 2-methyldiphenylmethyl ether	Disipal is the hydrochloride
PHENMETRAZINE	
Tetrahydro-3-methyl-2-phenyl-1 : 4-oxazine	Preludin
PIPAMAZINE	
10-[3-(4-Carbamoylpiperidino)propyl]-2-chlorophenothiazine	
PROTHIPENDYL	
10-(3-Dimethylaminopropyl)-9-thia-1 : 10-diazaanthracene	Phrenotropin is the hydrochloride
SULPHASALAZINE	
4-Hydroxy-4′-(pyrid-2-ylsulphamoyl)azobenzene-3-carboxylic acid	Salazopyrin
THIAMBUTOSINE	
N-*p*-Butoxyphenyl-*N*′-*p*-dimethylaminophenylthiourea	4-Butoxy-4′-dimethylaminodiphenylthiourea
	Ciba 1906
THIOTEPA	
Tri-1-aziridinylphosphine sulphide	Triethylene thiophosphoramide

Index to the supplementary list

(See the above list for the full approved name and the chemical name) .. ..

Proprietary Name	*Approved Name Reference*
Aminacyl B-PAS	Calcium Benzamidosalicylate
Ciba 1906	Thiambutosine
Crodimyl	Methylchromone
Decadron	Dexamethasone
Deronil	Dexamethasone
Dexacortisyl	Dexamethasone
Disipal	Orphenadrine
Esidrex	Hydrochlorothiazide
Etisul	Ditophal
Hydrenox	Hydroflumethiazide
Hydro-Saluric	Hydrochlorothiazide
Ilidar	Azapetine
Incidal	Mebhydrolin
Naclex	Hydroflumethiazide
Phrenotropin	Prothipendyl
Preludin	Phenmetrazine
Rontyl	Hydroflumethiazide
Salazopyrin	Sulphasalazine
Therapas	Calcium Benzamidosalicylate
Vespral	Fluopromazine
Vesprin	Fluopromazine

Company finance

Imperial Chemical Industries' turnover in 1958 was £463 million, the same as in the previous year, but profits before tax dropped to £44,513,794, a decline of nearly £11 million compared with 1957. The sharp fall in profits is due to lower prices; the profit/sales ratio has declined to 8·7% compared with 12·9% two years ago. The total Ordinary dividend is 8%, equivalent to the previous year's dividend.

Net profit of **Ilford Ltd.** for the year ended October 31, 1958, was £752,316 (£788,615). A final Ordinary dividend of 11%, making a total of 16% less tax, was recommended.

Hickson and Welch (Holdings) Ltd. have attained the highest profit in their history, while capital expenditure is greater than ever before. Net profit for the year ended September 30, 1958, was £248,553 (£251,397). A final Ordinary dividend of 9½% was declared.

Net profit of **John Knight Ltd.** for the year ended December 31, 1958, was £161,520 (£221,081). An Ordinary dividend of 50%, free of tax, has been recommended.

Consolidated net profit for **Unilever Ltd.** and **Unilever N.V.** for the year ended December 31, 1958, was £47·3 million (£40·3 million).

In the case of Unilever Ltd a dividend is recommended of 2s. 1·2d. actual per £1 of stock before deducting income tax (2s. 3·6d.), making 4s. 2·4d. per £1 of stock for the year ended December 31, 1958 (3s. 6d.), while for Unilever N.V. a dividend of 9¼% actual (10¼%), being the equivalent of the Unilever Ltd. dividend calculated in accordance with the Equalisation Agreement between the two companies, making 18½% for the year ended December 31, 1958 (1957-15½%).

Meetings

The Chemical Society

CAMBRIDGE

April 27. "Alkaloid Chemistry," by Dr. G. Smith. 5 p.m. The University Chemistry Laboratory, Lensfield Road.

HULL

April 28. "Recent Developments in Organometallic Compounds," by Prof. G. E. Coates. 5 p.m. Organic Chemistry Lecture Theatre, the University.

IRISH REPUBLIC

April 29, *May* 1 *and May* 4. "A Generation of Chemotherapeutic Research," by Dr. F. L. Rose. To be held as follows: April 29, 7.45 p.m. Trinity College, Dublin; May 1, 7.45 p.m. University College, Cork; May 4, 7.45 p.m. University College, Galway.

May 8. "The Nature of the Active Centre of Chymotrypsin and Other Esterases," by Prof. H. N. Rydon. 7.45 p.m. Trinity College, Dublin.

NORTHERN IRELAND

May 5. "Nucleotides and Bacterial Cell-wall Constituents," by Prof. J. Baddiley. 5.45 p.m. Queen's University, Belfast.

SOUTHAMPTON

April 24. "Nitrogen-containing Sugars," by Prof. M. Stacey. 7 p.m. Chemistry Department, the University.

Pharmaceutical Society

April 15. "Progress in the Chemistry of Natural Products," by Dr. J. B. Stenlake. 7.30 p.m. 17 Bloomsbury Square, London, W.C.1.

Society of Cosmetic Chemists

April 15-17. British Congress of Cosmetic Science. University College, London, W.C.1.

Institution of Chemical Engineers

April 28. A.G.M. and dinner. Park Lane Hotel, Piccadilly, London, W.1.

May 11-13. Symposium on "Instrumentation and Computation in Process Development and Plant Design," Central Hall, Westminster, London, S.W.1. Details from: The Gen. Sec., 16 Belgrave Square, London, S.W.1.

Society of Chemical Industry

CHEMICAL ENGINEERING GROUP

April 15. "Electrical Engineering in the Chemical Industry," by D. Birch. 6.30 p.m. College of Technology, Suffolk Street, Birmingham 1.

MICROBIOLOGY GROUP

May 7. Visit to Central Research Dept., Distillers Co. Ltd., Epsom. 2 p.m.

Royal Institute of Chemistry

April 24. Symposium on Separation Processes in Analytical Chemistry. 10.30 a.m. Inorganic Chemistry Lecture Theatre, South Parks Road, Oxford.

April 27. Ladies Evening. "Cosmetics," by R. H. Marriott. 7 p.m. 21 Albemarle Street, London, W.1.

New examinations rules

The City and Guilds of London Institute and the Institute of Science Technology have taken steps to rationalise their examinations and qualifications for science laboratory technicians. Hitherto, both Institutes have held examinations for science laboratory technicians, but in future there will be only one series of examinations, held by the City and Guilds of London Institute on behalf of both Institutes.

Transitional regulations have been agreed to ensure that no student at present preparing for the examinations of the Institute of Science Technology suffers because of the new arrangements. The arrangements for the award of the Fellowship of the Institute of Science Technology remain as hitherto.

Analysts elect officers

At the 85th a.g.m. of the Society for Analytical Chemistry held in London last month, the following Officers and Members of Council were elected for the forthcoming year:

President: R. C. Chirnside;

Past Presidents serving on the Council: J. H. Hamence, D. W. Kent-Jones, J. R. Nicholls, K. A. Williams;

Vice-presidents: D. C. Garratt, Magnus A. Pyke, J. G. Sherratt;

Hon. Treasurer: A. J. Amos;

Hon. Secretary: R. E. Stuckey;

Hon. Assistant Secretaries: L. Brealey (Programmes), S. A. Price.

Other members of the Council are: N. L. Allport, H. E. Brookes, R. A. Chalmers, W. T. Elwell, C. H. R. Gentry, J. Haslam, E. I. Johnson, G. W. C. Milner, R. F. Milton, F. C. J. Poulton, T. S. West and C. Whalley.

Cosmetic Chemists annual dinner

Over 200 members and guests, a record number, attended the annual dinner and dance of the Society of Cosmetic Chemists of Great Britain held in London recently.

At the dinner Dr. R. H. Marriott, President of the Society, mentioned the proposal of the American Society that an international association of cosmetic societies should be formed; this had led to the formation of a German Society which had organised a conference in September 1958, at which the foundations of an International Federation were laid. The other European cosmetic societies include those of Switzerland, France, Belgium, Italy and Denmark and a new one in Spain.

The principal guest was Mr. F. Schon, chairman of Marchon Products, and other prominent guests included Mr. and Mrs. G. Keller, the former being a member of the American Society and President of the Essential Oil Importers' Association, and Mr. van Amerigen.

The new wing of the I.C.I. Alkali Division research laboratory (right foreground). In the background is the Division's Winnington Works.

New number

The telephone number of Gale and Mount Ltd., Commerce Road, Brentford, has been changed to: Isleworth 4334-5.

Change of address

Kingsley and Keith Ltd. have moved to new premises at Rex House, 38 King William Street, London, E.C.4. Telephone Mincing Lane 1101-6.

Tour of U.K.

Mr. H. Rassman, the export manager of Dragoco G.m.b.H. of Holzminden, W. Germany, is now on a business tour of the United Kingdom.

Bruce Starke and Co. Ltd., of 5 Fenchurch Street, London, E.C.3 (Telephone: Mansion House 3586), are the agents for the company and Mr. Rassman may be reached through them.

New 'Arcton' numbering system

To assist customers, I.C.I. has decided to re-code its *Arcton* range of refrigerants and propellents. Manufacturers of chlorofluorohydrocarbons use a variety of numbering systems to distinguish grades of different chemical composition. I.C.I.'s decision will simplify the position as the system to be adopted by the company is now widely used in the U.S.A. and elsewhere.

As from May 1959 *Arcton* grades will be re-numbered as follows:

Arcton		*Arcton*
9	to be	11
6	,, ,,	12
3	,, ,,	13
7	,, ,,	21
4	,, ,,	22
63	,, ,,	113
33	,, ,,	114
50	,, ,,	133a

Extension to I.C.I.'s Winnington research department

New laboratory extensions to the research department of I.C.I. Alkali Division at Winnington, Cheshire, were opened on March 4, by Sir Cyril Hinshelwood, President of the Royal Society.

It was in these laboratories in 1933 that polythene was discovered.

The new 20,000 sq. ft. laboratories, will increase laboratory space available to the research department by approximately a third. The extensions are housed in a three-storey building running parallel with, and connected to, the present block of research laboratories. The narrowness of the site has dictated the layout of the new building, so that laboratories and offices are on one side only of the longitudinal corridors.

The ground floor houses the semi-technical and development stages that usually follow laboratory-scale research in the establishment of new products and processes. The two upper floors, which accommodate about 60 graduate scientists and their assistants, have been designed to allow some flexibility in their layout, *e.g.*, benches can be resited without interfering with service outlets.

New N.R.D.C. chief

Mr. J. C. Duckworth, B.A., F.INST.P., A.M.I.E.E., F.INST.F., has been appointed managing director of the National Research Development Corporation. This is a statutory appointment made by the Board of Trade under the Development of Inventions Act, 1948. Mr. Duckworth is 42. After taking First Class Honours in Physics at Oxford in 1938, he played a leading part in radar research and development during the war. After the war, he was engaged in fundamental nuclear physics research at Chalk River in Canada and at Harwell.

News from Abroad

FRANCE

New chemical plants in operation

A new complex of chemical plants has been brought into operation by S.A. des Produits Chimiques Saint-Gobain at their plant at Berre, near Marseille, adjacent to the oil refinery of Compagnie de Raffinage Shell-Berre. The new facilities will enable Shell Saint-Gobain, in which the Royal Dutch/Shell group of companies has a 60% interest, to manufacture *Epikote* resins, carbon black and base materials for detergents, as well as to expand their range of organic solvents.

SWITZERLAND

Du Pont Sales H.Q.

A Swiss sales company, Du Pont de Nemours International S.A., with H.Q. in Geneva, has been formed by E. I. du Pont de Nemours and Co. Inc.

The company will sell products to be made by Du Pont subsidiaries in Europe, and many products made in the U.S. by the parent company. At first it will sell textile fibres and elastomers. Other products will be added later. The new company will conduct its own merchandising, advertising, and product promotion programmes.

Geneva was chosen as H.Q. for the company because it is near to Du Pont's European distributors and customers; and because Switzerland is a centre for international trade.

David H. Conklin, European director of Du Pont's International Department, and Jean Dutoit and H. P. Brechbuhl of Geneva, constitute the board of the new company.

Du Pont's first European plant, near Londonderry, Northern Ireland, will make neoprene synthetic rubber; it is due to start up next year. The company's first plant on the Continent, now being built in Malines, Belgium, to produce paint for the Common Market, will be completed later this year. A third project is an *Orlon* acrylic fibre plant which is to be built Dordrecht, Holland.

Cyanamid's basic research institute

Cyanamid International have completed plans for a basic research laboratory, to be named Cyanamid European Research Institute Inc., to be located in Geneva. The new centre will employ British, Swiss, French, German and other European scientists and will be devoted solely to long-range research in chemistry and biology. According to Dr. Robert C. Swain, the company's vice-president for Research and Development, the Institute will not be an industrial laboratory but will be designed to add to the world's scientific knowledge.

Dr. Swain said that it was planned to employ six or seven senior scientists selected from different scientific fields. Each would become the head of a department fully staffed and equipped with modern facilities to permit him to continue and expand his personal scientific interests.

Speaking of the company's research, Dr. Swain mentioned that the first total synthesis of a tetracycline, biologically active and related to aureomycin, had recently been achieved. He said that this "could lead to the construction of new antibiotics, all of which heretofore have been derived from living organisms."

The Institute has acquired an 8½ acre tract of land in the Cologny section overlooking Lake Geneva. A large residence is included which will be converted and enlarged.

CANADA

Albright and Wilson subsidiary's new plant

Dr. David E. Jones, president of the Electric Reduction Co. of Canada Ltd.—producers of phosphorus and phosphates, and one of the Albright and Wilson group of companies—has announced a multi-million dollar project to expand and diversify the company's production. At Port Maitland, Ontario, ERCO are to build new plants to produce sulphuric and phosphoric acids, as well as sodium phosphates and other products, to fill the needs of industry and agriculture in Eastern Canada. Construction will start almost immediately and production should begin early in 1960.

Phosphoric acid is the starting-point for high analysis fertilisers, and S.W. Ontario is the major and growing market in Canada for such fertilisers, which have until now relied on large quantities of imported raw materials. Phosphates are important for the detergent industry as well as for metal finishing and food processing. The concentration of these industries in Central Ontario makes Port Maitland the logical site for the new plant. It lies at the point where Grand River enters Lake Erie, and has excellent rail, road and deep water transport facilities.

The recent expansion of ERCO's sodium chlorate production in Buckingham (Quebec Province) and in Vancouver (British Columbia) made it the largest producer of sodium chlorate in the western world.

NIGERIA

Allenbury's new building

The new office building and showrooms of Allen and Hanburys (Nigeria) Ltd. was opened in Lagos recently. The Hon. Ayo Rosiji, Minister of Health, performed the opening ceremony which was attended by C. W. Maplethorpe, managing director of Allen and Hanburys Ltd., and R. C. Irving, chairman of the Nigerian company.

DOMINICAN REPUBLIC

Pharmaceutical market

A report on the retail pharmaceutical outlets in the Dominican Republic states that for a country of 2,700,000 inhabitants there is a very brisk trade both in home-produced and imported pharmaceuticals. The biggest volume of business is done in the 300 shops of the capital, Ciudad Trujillo. The standard is high and will become higher with the University Pharmacy Course extended from three to five years.

The two principal manufacturing firms, with a wide range of products, are Labatorios Quimicos Dominicanos and La Farmaceutica Celia Cruz.

The Government health programme, with a budget of over £2 million annually, and a rapidly rising population, expected to reach three million by 1960, both combine to make this a market worth exploring.

SOUTH AFRICA

Pfizer's new depot

The Pfizer Corp. of America is to build a factory on a 5½-acre site which its South African subsidiary has bought in the industrial area west of Johannesburg. The factory is likely to become one of the corporation's main world depots.

"Monopoly" charge

The Government has been asked to enquire under the Monopolies Act into the distribution of ethical products and medicines. In the past ethical products had been imported by a number of independent wholesale chemists and distributed to retail chemists. Recently, however, all these wholesale chemists in Johannesburg, Durban, Port Elizabeth, Bloemfontein, Cape Town, and, it is understood, also in Rhodesia, were taken over by one financial institution. The result was that the wholesale trade in medicine and ethical products was now controlled from one office. This was said to be a most alarming position.

Expensive medicines to be examined

It is expected that the South African Government will institute an enquiry into the cost of drugs and medical fees. The enquiry is expected to examine charges that the cost of illness is becoming too much for the "man-in-the-street." The main aim will be to discover why imported medicines—particularly antibiotics—are so expensive in the Union. Some sell at three times their overseas price.

Drug prices in the Union, which are among the highest in the world, are laid down by the pharmaceutical distribution houses. These prices are binding on chemists and druggists and on medical practitioners. One reason for the high prices is the intense competition among more than 40 drug distributors to promote and advertise their brands.

It was said that 60% of all retail chemists were controlled by the one monopoly.

A monopoly like this could put pressure on overseas firms as far as the prices and profit margins on their products were concerned. Overseas firms had already shown that they did not like the new situation.

Some British and American firms had already decided to produce their products locally and to control the distribution themselves because of the new position.

Insecticide company increases turnover

The annual report of Klipfontein Organic Products Corporation, a State undertaking, for the year ended June 30, 1958, reveals an increase in turnover from £1,260,000 to £1,440,000. Out of a net profit of £74,460, £25,265 was provided for taxation. Capital and reserves totalled £2,289,440. The Corporation is seeking more capital on a "sounder basis."

During the financial year capital expenditure of £537,382 was incurred. The output included over 4,000 tons of technical DDT and BHC.

From the material made, 5,600 tons of wettable and dusting powders and 270,000 gal. of emulsions and liquid insecticides were produced.

Altogether 55 different insecticides were manufactured. When the demand warrants it the Corporation will consider manufacturing the basic materials of chlorinated-camphene and organic-phosphorus ranges, such as toxaphene and diazinon. "At present," states the annual report, "a new insecticide is being tested out which is not at all toxic to man or beast." The basic materials for herbicides, especially against jointed cactus, are still being imported by the Corporation, but it is investigating the production of the materials when the demand warrants it.

During the year 12,500 tons of caustic soda and other chemicals were produced. The value of exports of Klipfontein products to other African territories amounted to £133,000. Finance, however, is one of the worries of the directors. "Due to insufficient capital the Corporation has been obliged to arrange a loan with its bankers in order to finance capital expenditure in connection with essential developments."

UNITED STATES

Materials research

A new Division on Materials Sciences will be organised by the American Society for Testing Materials to co-ordinate and intensify the development of knowledge of the fundamentals of materials. The new division, the first to be established by ASTM, will augment in depth and scope the Society's objectives of promoting knowledge of engineering materials and tapping new sources of knowledge for the Society's standardisation activities. The division will concern itself with the collection, establishment and publication of basic information essential in creating a better understanding of materials and their properties, and especially will help to answer "why" materials are what they are.

Millions for research

Chemical producers in the United States are expected to spend at least $87,025 million to construct new laboratories in 1959 and 1960, according to results of the annual construction survey conducted by the Manufacturing Chemists' Association. This figure includes an estimated $59·6 million for projects under way and $27·425 million for additional facilities planned in the near future. In addition to this outlay, chemical research laboratories costing approximately $70·145 million were completed in 1958, bringing the total expenditures for chemistry laboratories to $157·170 million for the three-year survey period, 1958-60.

The Association has reported that the chemical industry's total budget, including operating costs for basic and applied research, rose about 6% in 1958—again despite the recession—to an estimated $560 million. This includes government-financed research. The industry's privately-financed research budget of $543 million is the highest in the nation, however.

The chemical industry's expenditures for basic research alone represent about 10% of the industry's over-all research budget. The National Science Foundation has reported that the chemical industry's basic research programme accounts for about 25% of the cost of all basic research financed by all U.S. industry.

Award for synthesising penicillin

An award for his achievements in synthesising penicillin and for research in the synthesis of peptides was made to Dr. John C. Sheehan of the Massachusetts Institute of Technology at the annual meeting of the American Chemical Society in Boston, April 5-10. A $1,000 prize, the award is given annually in recognition of "creative work in synthetic organic chemistry."

The announcement that he had succeeded in synthesising penicillin was made by Dr. Sheehan two years ago. At the ACS meeting he reported on further accomplishments in this field and also in the development of a selective method for synthesising peptides, using carbodiimide as a key reagent.

Cosmetic chemists honour dermatologist

The Special Award presented annually by the Society of Cosmetic Chemists, and carrying a prize of $1,000, will be awarded this year to Dr. Irvin H. Blank in recognition of his fundamental research and writings on factors controlling suppleness and flexibility of skin. The distinguished dermatologist and biochemist will attend the May 7 meeting of the Society to receive the award.

Dr. Blank was among the first to recognise, demonstrate and publicise the fact that moisture is the primary factor in keeping skin soft, smooth and supple.

AUSTRALIA

Petro-chemicals industry planned

A £23 million petro-chemical industry is to be established in Victoria. The Vacuum Oil Co. Pty. Ltd., Union Carbide Australia Ltd., C.S.R. Chemicals Pty. Ltd., the Distillers Co. of London and the Dow Chemical Co. of America plan four plants—one to make ethylene and butadiene, one for the manufacture of synthetic rubber, one to produce polyethylene, and one to make styrene. Construction of the new plants is expected to begin this year.

I.C.I. spends £3·5m

Imperial Chemical Industries of Australia and New Zealand Ltd. and its subsidiaries spent more than £3,500,000 on construction work during 1958. Extensions were made to nearly all major factories, and new projects and extensions completed included a plastics technical service laboratory at Ascot Vale, a new phthalic anhydride plant for the Newcastle Chemical Co., extensions to the polythene plant and to the *Visqueen* factory, new hydrochloric acid plants at Botany and Yarraville, and a new nitric acid plant at Nobel.

New Products

" Husk " vaccine

Husk or hoose, a disease caused by a parasitic worm (*Dictyocaulus viviparus*) in the lungs of cattle is a serious disease of cattle in Great Britain today, and is a source of considerable economic loss. As a result of collaboration between workers at Glasgow University and the Research Division of Allen and Hanburys Ltd., an effective vaccine designed to protect animals against this disease is now available.

The vaccine will be distributed under the name of *Dictol*, and is said to represent an entirely new conception of a prophylactic medicine, as not only is it the first vaccine to prevent husk, but it is also the first vaccine to give protection against a metazoan parasite and is, therefore, of significance to both human and veterinary medicine.

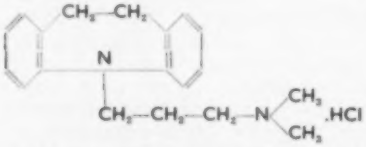
The vaccine is an aqueous suspension of larvæ of *D. viviparus* partially inactivated by X-rays. It is given by mouth. Although this means that it will be easier to administer than other vaccines which are injected, it will be issued to the veterinary profession only and not put on general sale.

" Green note " for perfumers

Vertilal C is a new " green note " devoted by Dragoco and is said to reproduce the fragrance of young green foliage. A colourless liquid, the product is soluble in mineral oil in any proportion and has a solubility in alcohol of 2% in 60% by volume; it is also said to be well tolerated in creams and to be alkali proof for both white and coloured soaps. The manufacturers recommend it particularly in compounds for perfumes, toilet waters, shampoos and soaps.

Combating melancholia

A new iminodioenzyl derivative, *Trofranil*, is available, to mental hospitals only, from the Geigy Pharmaceutical Co. Ltd. Chemically it is N-(γ dimethyl-aminopropyl)-iminodibenzyl hydrochloride and has the following structure:



According to the manufacturers the product regulates the basic depressive disorder and helps the patient to bring order into his emotions, producing both subjective and objective improvement in depressive states.

The drug is available as either sugar-coated tablets of 25 mg. or as ampoules each containing 25 mg. in 2 ml.

Hand cream

Apiella Royal Jelly hand cream has been introduced by F. Farthing and Co. Ltd. in standard 1 oz., and boudoir 4½ oz. sizes. Trade prices per doz. are £1 8s. 6d. plus 16s. 8d. Purchase Tax, and £4 6s., plus £2 10s. 4d. Purchase Tax respectively.

Anti-thyroid drug

Neo-Mercazole (carbimazole), a product of British Schering Ltd., is said to be less likely than other anti-thyroid agents to cause hyperplasia or increased vascularity of the gland. Initial dosage varies between 15-45 mg. daily depending on the severity of the case, and maintenance dosage will usually be between 2·5 and 15 mg. daily.

The product is available as scored tablets each containing 5 mg. of carbimazole in containers of 100 and 500.

Hibitane for solutions

Hibitane chlorhexidine digluconate solution 20% w/v is available from Imperial Chemical Industries Ltd. (Pharmaceuticals Division). The more soluble digluconate salt is said to possess the antibacterial properties exhibited by other *Hibitane salts* and is presented as a 20% w/v aqueous solution, suitable for preparing simple solutions of *Hibitane* and for use in formulations where a soluble salt is required.

Prices are: bottles of 100 ml., 16s. 6d. each retail, 132s. doz. trade, and bottles of 500 ml. 78s. each and 624s. doz. trade.

Treating dermatoses

Said to be indicated in the treatment of acute or chronic dermatoses with an allergic or inflammatory basis, *Dequalone-P*, made by Allen and Hanburys Ltd., contains *Dequadin* (dequalinium) chloride 0·4% and prednisolene 0·25% in a bland, non-irritating hydrophilic base which is non-greasy and which is claimed not to stain the skin or clothing.

According to the manufacturers the product is rapidly effective in the management of contact dermatitis, neuro-dermatitis, stasis dermatitis, seborrhœic dermatitis and intertrigo. Eczemas of various types including allergic eczema, infantile eczema and varicose eczema are also said to respond to it. Its anti-pruritic effect is valuable in the prevention of " reflex rubbing " or scratching which often causes the development of secondary infection.

The product is supplied in tubes each containing 5 g., trade price 3s. 9d. each, exempt from tax.

Diuretic-antihypertensive agent

Said to be up to 15 times more effective than chlorothiazide, *Esidrix*, a new product available from Ciba Pharmaceutical Products Inc., is also claimed to potentiate the action of other antihypertensive drugs. The product, which chemically is hydrochlorothiazide, is said to effectively control the œdema which accompanies congestive heart failure in doses of 50 mg. twice daily.

Softening agent for hair and skin

A cationic type emulsifying agent claimed to impart softness to hair and skin is available from the Du Pont Co. Called *Avitex ML Softener*, it should be of value in formulations utilising dry ingredients such as stearic acid. Small concentrations of the product, according to Du Pont tests, help prevent the extremely dry feel of preparations containing high concentrations of stearic acid and also reduce the tendency of such products to " roll out " when rubbed on the skin.

The softening agent is said to be mildly bactericidal, efficient over a wide *p*H range, and to blend well with other cationic or non-ionic agents. According to the manufacturers it is also a good carrier medium for other ingredients in creams and lotions.

Combined vitamin and mineral supplement for poultry

What is claimed to be the first combined vitamin and mineral food supplement for poultry with a guarantee of vitamin stability for 12 months from manufacture is now being marketed by Boots Pure Drug Co. The new supplement, *Vita-Mindif for Poultry*, replaces *Mindif* Mineral Salts for Poultry, and eliminates the need for separate mixing of *Drivite* (vitamins A and D_3).

The problem of combining vitamins and minerals in a single food supplement for poultry with a good storage life has occupied Boots for more than three years. Early tests showed that, even with protected vitamins, interaction set up oxidation which could reduce potency in anything from a few hours to a few weeks. They now claim to have eliminated the effects of oxidation for at least 12 months without altering the balanced mineral salts formula. Stocks not sold well within the safety period will be regularly withdrawn from Boots shops.

Vita-Mindif for Poultry is sold at 32s. per 60 lb. pack which is sufficient for one ton of feed. This compares with 33s. 2½d. per ton of feed when *Mindif* mineral salts and *Drivite* were used separately.

Fuel oil additive

A Du Pont Co. fuel oil additive, *FOA*-2, is claimed to eliminate and prevent formation of sludge. Said to be usable in all types of distillate fuel oils, including blends, the product is added to the fuel oil in the storage or work tank at the rate of about 20 to 40 lb. per 1,000 bls. of oil.

Eye-drop cream

British Schering Ltd. are manufacturing an eye-drop cream containing 0·5% hydrocortisone acetate with 10% *Albucid* (sulphacetamide sodium). Named *Cortucid*, the product is said to reduce inflammation without the increased risk of infection normally associated with hydrocortisone therapy. Packed in a collapsible tube, the active ingredients are incorporated in a water-miscible fluid cream.

Quaternaries patented

Gallowhur Chemical Corp. Ossining, N.Y. has been issued a patent (U.S. 2,865,805) on a series of quaternary ammonium compounds which are cited as having useful pesticidal properties. The compounds, which are reaction products of certain quaternaries and naphthalene or naphthol sulphonic acids, are water-insoluble.

Potential applications claimed include use as durable, non-leaching fungistats for textiles and as agricultural pesticides.

Oral analgesia

An oral analgesic claimed to be as potent as morphine, more efficacious than pethidine and less liable than either to produce untoward reactions is available from Burroughs Wellcome and Co. Known as *Pipadone*, each tablet contains dipipanone hydrochloride, 25 mg., and cyclizine hydrochloride (*Marzine*) 50 mg. It is stated that the combination of cyclizine with dipipanone virtually excludes the side-effects of nausea and vomiting, allowing potent analgesia to be achieved by oral administration.

The tablets are issued in bottles of 50 and 250 at prices of 15s. and 72s. respectively, subject to tax.

Thiolated gelatin

Schwarz Laboratories, Inc., announce the first of a series of thiolated gelatins, *Thiogel*-20. The thiolation of gelatin (addition of free sulphydryl (SH) groups) enlarges the molecular structure and new properties are developed. One is the ability to form a gel rapidly, without the necessity of chilling.

A white powder in the dry state, thiolated gelatin may be used for vehicles for pharmaceuticals, preparation of absorbent surgical sponges, and as protective agent against radiation. In cosmetics it may be used for hair-setting bases and in biochemistry for enzyme stabilisation.

Pharmaceutical Recruiting Film

This is a shot from a film "Pharmacy and You," made by Boots Pure Drug Co. Ltd., to stimulate recruitment to retail pharmacy. This shot is from the opening sequences illustrating some phases in the history of medicine; it portrays what could go wrong in the ancient remedy of a steam bath. The film, which runs for 20 min., shows how a young man enters pharmacy, following him through school, college and locum training, and ending with him taking charge of a pharmacy. Many scenes were filmed at the Bristol College of Pharmacy and students and teaching staff played parts in the film. The leading character was played by a young pharmacist. Boots have deliberately avoided advertising in this film and offer it free for showing to schools and similar audiences. Boots have also produced a 10 min., film illustrating their many activities—research, manufacturing and retailing. This can also be borrowed free.

NEW COMPANIES

These particulars of new companies have been extracted from the daily register of Jordan and Sons Ltd., company registration agents, Chancery Lane, London, W.C. 2.

Felton Co. (Great Britain) Ltd. 21.1.59. Audrey House, Ely Place, London, E.C.1. Production, manufacture, purchase, sale, importing, storing, marketing and exporting of all industrial chemicals, etc. £100. Dirs.: L. L. Gefen and R. W. Stansfeld.

James Foster (Chemists) Ltd. 21.1.59. 17 Breck Road, Poulton-le-Fylde, Lancs. £3,000. Dirs.: Mrs. I. H. Dunderdale and H. Rigby.

A. C. Stockwell and Son Ltd. 22.1.59. 22 The Green, Ealing, London, W.5. To take over bus. of chemist, druggist photographic and fancy gds. dlr. cd. on at Ealing by A. C. Stockwell, etc. £3,000. Dirs.: A. C. and C. J. Stockwell.

G. Briggs and Co. Ltd. 23.1.59. 8 Railway Street, Brierfield, nr. Burnley. To take over bus. of chemists and druggists cd. on at Brierfield by W. and Mona Petty and J. P. Steel. £3,000. Dirs.: W. and Mrs. M. Petty and J. P. Steel.

Liss Products Ltd. 27.1.59. Gamage Bldg., 118 Holborn, London, E.C.1. Chemists and druggists. £100. Dirs.: H. and Edith Liss.

Texylon (Great Britain) Ltd. 4.2.59. Mnfrs., mchts. and importers of chemicals and dyestuffs, etc. £20,000. Dirs.: not named. Sub.: E. A. Levine, 9 Netherall Gardens, Hampstead, London, N.W.3.

Biokosma (England) Ltd. 6.2.59. Mnfrs. and mchts. of perfumery, cosmetics, etc. £100. Dirs.: K. Strebel, Poultons, Dormansland, Surrey, M. Steidle and H. Lake.

M. E. Martin (Chemists) Ltd. 9.2.59. 350 Leyland Lane, Leyland, Lancs. £2,500. Dirs.: Francis C. Martin and Mrs. M. E. Cardwell.

Tom E. Hobson Ltd. 9.2.59. 46 Crooked Billet, London, S.W.19. To take over bus. cd. on at 46 Crooked Billet, S.W.19, by Tom Hobson and to carry on bus. of chemists, druggists, etc. £100. Dirs.: T. E. Hobson and F. Perkins.

Yorkshire Anti-Corrosive Co. Ltd. 10.2.59. 16 Princes Street, Harrogate. Mnfrs. and dlrs. in chemical products. £1,000. Dirs.: S. and Joan A. Kiddle.

Deneway Pharmacy Ltd. 10.2.59. £300. Dirs.: E. and Mrs. M. Priddle, E. and Joan Barker, all of "Pamellia," Hillbrow, Hove.

Amnio Ltd. 11.2.59. 59 New Cavendish Street, London, W.1. Dlrs. in and shippers of cosmetics, skin foods, perfumes, etc. £100. Dirs.: not named. Sub.: J. E. Norton, 116 Old Broad Street, London, E.C.2.

Arnolds Chemists Ltd. 11.2.59. 14 Allhalland Road, Bideford, Devon. £100. Dir.: D. L. S. Taylor.

John Hugall Ltd. 12.2.59. 143 Northenden Road, Sale, Cheshire. To take over bus. of pharmaceutical chemist and optician cd. on at Sale, Ches., by J. Hugall, etc. £1,000. Dirs.: J. and Lillian M. Hugall.

THE CHEMICAL MARKET

ZINC OXIDE CHEAPER; OILS AND WAXES UP

LONDON.—**Zinc oxide** is now £109 per ton in 2-ton lots, a decrease of £1 10s., while **2 : 4 D acid** has decreased by £10 to £320 per ton. **Calcium chloride,** solid 70-72%, in 8-ton lots, is down 10s. 6d. to £16 10s. per ton, and **caustic soda** is down £1 4s. 6d. to £37 16s. 6d. per ton in 1-ton lots. **Red mercury iodide B.P.C.,** in 28-lb. lots, has increased by 1s. 3d. to £1 8s. 4d. per lb. and **ferri ammonium citrate B.P.,** scales and granules, by 1½d. to 4s. 7d. and 3s. 9d. per lb. respectively. **Bismuth oxide B.P.C.,** in 28-lb. lots, is down 5d. to £1 6s. 10d. per lb., **calcium lactate B.P.,** in 1-cwt. lots, by 7d. to 2s. 4d. per lb., **silver nitrate,** in 500 g. lots, by 1½d. to 5s. 1½d. per oz., and **strychnine alkaloid,** in 25-oz. lots, to 8s. per oz.

FINE CHEMICALS

Acetanilide 12½ kg. 7s. 4d. kg.
Arsenious oxide B.P.
7-lb. lots 1s. 9d. lb.
1-cwt. lots 1s. 2d. lb.
Ascorbic acid
100 kg. £4 14s. kg.
Aspirin
56 lb. 5s. 2d. lb.
1-cwt. 4s. 11d. „
5-cwt. lots 4s. 9d. „
Atropine
Sulphate, 500 g. £59 18s. 6d. kg.
Alkaloid, 500 g. £69 10s. kg.
Benzene B.P.C. 28-lb. lots 1s. 8d. lb.
Benzoic acid 12½ kg. 7s. 4d. kg.
Benzyl benzoate
According to pack 5s. to 5s. 6d. lb.
Bismuth oxide B.P.C. 1934
28-lb. lots 26s. 10d. lb.
Bismuth salts 28-lb. lots:
Carbonate 22s. 3d. lb.
Subgallate 21s. 1d. „
Salicylate 21s. 9d. „
Subnitrate 20s. 5d. „
Borax B.P.
Powder £57 10s. ton
Extra fine £58 10s. „
Boric acid B.P.
Crystal £93 10s. „
Powder £93 „
Bromine B.P.C. 7-lb. lots 6s. lb.
Caffeine 50 kg. 42s. 6d. kg.
Calamine 50 kg. 4s. kg.
Calcium gluconate
1 cwt. lots dlvd. 3s. 7d. lb.
Calcium glycerophosphate
50 kg. 28s. 6d. kg.
Calcium lactate B.P.
7-lb. lots 2s. 11d. lb.
1-cwt. lots 2s. 4d. „
Chloral hydrate 50 kg. 10s. kg.
Citric acid, B.P. Powder or granulated:
1-cwt. lots £11 5s. cwt.
5-cwt. lots £11 „
Codeine
Alkaloid 100 g. £138 10s. kg.
Phosphate 100 g. £110 „
Cream of tartar
1-cwt. lots £11 15s. cwt.
5-cwt. lots £11 13s. „
Ephedrine
Hydrochloride 3 kg. £7 1s. 1d. kg.
Alkaloid 3 kg. £12 7s. kg.
Sulphate 3 kg. £7 1s. 1d. „
Eucalyptol
1-cwt. lots 11s. lb.
5-cwt. lots 10s. 6d. „
Ferri ammonium citrate B.P.
1-cwt. lots, scales 4s. 7d. lb.
1-cwt. lots, granules 3s. 9d. „
Ferrous gluconate
1-cwt. lots dlvd. 6s. 3d. lb.
Gallic acid B.P.C.
1-cwt. lots 10s. „
Gluconic acid technical 50%
Minimum 12-gal drums
19s. gal., drums extra, returnable
Glucono delta lactone
1-ton lots delvd. 5s. net lb.
Glycerophosphoric acid
24 litres 11s. 10d. litre
Glycine (amino acetic acid)
12½ kg. 18s. 10d. kg.
Hexyl resorcinol 10 kg. £7 10s. kg.
Hydroquinone 12½ kg. 23s. 10d. kg.
Iodides
Ethyl 4 kg. bottles 62s. 9d. kg.
Mercury, red B.P.C.
28-lb. lots 28s. 4d. lb.
Potassium B.P.
28-lb. lots 8s. 0d. „
Sodium B.P.
28-lb. lots 13s. „
Iodine, Chilean crude,
99% min. in wooden casks 15s. kg.
Iodoform
12½ kg. and under 50 kg. 42s. 6d. kg.
Lactose 50 kg. 3s. 2d. kg.
Lithium salts 5-cwt. lots
Benzoate 10s. lb.
Carbonate B.P.C. 11s. 3d. „
Chloride (commercial) powder
11s. „
„ granular 10s. 9d. „
Hydroxide 9s. 9d. „
Citrate B.P.C. 9s. „
Sulphate 8s. 6d. „
Salicylate, 10 cwt., dlvd. 9s. 9d. „
Magnesium carbonate B.P.
Light cwt. lots dlvd. £129 ton
Magnesium trisilicate 28-lb. packs
28-lb. lots 4s. 3d. lb.
1-cwt. lots 3s. 10d. „
5-cwt. lots 3s. 7d. „
Bulk rates for larger quantities are from 3s. 1d. lb. in 1-ton lots
Manganese hypophosphite B.P.C.
7-lb. lots 13s. 11d. lb.
1-cwt. lots 12s. 11d. „
Mercuric chloride B.P.
50-kg. lump 48s. 6d. kg.
Methyl salicylate 1-cwt. lots 3s. 3d. lb.
Morphine
Alkaloid, 100 g. £138 18s. 4d. kg.
Nicotinamide 1 kg. £3 15s. kg.
Nicotinic acid
12½ kg. 52s. 6d. kg.
1 kg. 55s. „
Oleine, B.P. extra pale, 3/4 cwt. drums returnable carriage paid G.B.
£160 ton
Phenolphthalein 50 kg. 24s. 3d. kg.
Phosphoric acid B.P.
(s.g. 1·750) 10-carboy lots 1s. 4d. lb.
Potassium permanganate B.P.
1-cwt. lots dlvd. 1s. 11¼d. lb.
Procaine hydrochloride (foreign) 2 kg. 59s. kg.
Quinine 1-oz. lots 4s. 4d. oz.
Riboflavin
100 g. 5¼d. g.
10 g. 7d. „
Saccharin
500 g. £7 4s. for this quantity
Salicylic acid
B.P., dlvd. 3s. 2½d. to 5s. 6d. lb.
Silver nitrate
500 g. 5s. 1½d. oz.
Sodium benzoate B.P.
1-cwt. lots 2s. 9½d. lb.
1-ton lots 2s. 7½d. „
Sodium gluconate technical
3-cwt. lots delvd. 3s. net lb.
Sodium salicylate
50 kg. 8s. 8d. kg.
12½ kg. 9s. „
Sodium thiosulphate
Crystals, photographic quality
1-ton lots 49s. cwt.
Stearic acid B.P.C. flake, carriage paid G.B. £154 ton
Strychnine 25 oz.
Alkaloid 8s. oz.
Hydrochloride 8s. „
Sulphate 7s. „
Sulphaguanidine
12½ kg. 33s. kg.
50 kg. 32s. „
Sulphanilamide
12½ kg. 16s. 6d. kg.
50 kg. 15s. 4d. „
Sulphathiazole 12½ kg. 39s. 9d. kg.
Tannic acid B.P. Levis
1-cwt. lots 10s. lb.
Tartaric acid B.P.
Powder or granulated,
10 cwt. or more £14 10s. cwt.
Terpineol B.P.
40-gal. drums 2s. 4½d. lb.
1-cwt. lots 2s. 7d. „
Theophylline B.P.
500 g. 27s. 6d. for this quantity
Thiamine hydrochloride
100 g. 4d. g.
1 kg. £11 15s. kg.
Thioglycollate
Ammonium 12s. 4d. to 16s. 4d. lb.
Calcium:
7-lb. lots 17s. 3d. „
5-cwt. lots 14s. 3d. „
α-Tocopherol 25-g. lots 1s. 1d. g.
Vanillin 25s. 6d. to 30s. 6d. lb.
Zinc oxide B.P.
2-ton lots £109 ton

GENERAL CHEMICALS

Acetic acid 1-ton lots dlvd.
80% Technical £99 ton
80% Pure £105 „
Glacial B.P. £114 „
99-100% Glacial £111 „
98-100% Glacial £108 „

Acetic anhydride
1-ton lots dlvd. £128 ton
Acetone
5-gal. drums, free, non-returnable £128 ton
40 to 45-gal. drums, 10-ton lots £88 „
Alum, potassium granular crystals
50 kg. 1s. 2d. kg.
Aluminium hydroxide B.P.C. 34
28-lb. lots 2s. 4d. lb.
Aluminium stearate
(Precipitate) 1-ton lots £253 6s. ton
Ammonia
Persulphate £6 2s. 6d. cwt.
Phosphate: Mono- £106 ton
Di- £100 „
Amyl acetate
B.S.S. 10 tons and over £251 ton
Technical £249 „
Amyl alcohol
Technical in 1-ton lots £260 ton
Arsenic White powdered ex store £42 ton
n-Butyl acetate
10-ton lots £173 ton
n-Butyl alcohol
10-ton lots £149 ton
Calcium chloride
Solid 70 to 72%, 8-ton lots dlvd. £16 10s. ton
Calcium oxide (Lime)
Ex marble 28-lb. lots 3s. 10d. lb.
Caustic soda
Solid 1-ton lots, from £37 16s. 6d. ton
Chloroform B.P. ½-ton lots 2s. 11½d. lb.
Chromic acid
Dlvd. U.K. (less 2½%) 2s. 0½d. to 2s. 0¾d. lb.
DDT 3s. 0½d. to 3s. 2d. lb.
2 : 4-Dichlorophenoxyacetic acid
99% pure, 1-cwt. bags £320 ton
Dimethyl sulphate 400 lb. drum lots 1s. 8d. lb.
Ether (Diethyl ether)
Tech. B.S.S. and Solvent B.P. 1-ton lots in drums 2s. lb.
Ethyl acetate 10-ton lots £145 ton
Ethyl alcohol
95% Gay Lussac 66·0 o.p.
2,500 to over 300,000 proof gallons per year in tank wagons 4s. 2¾d. to 4s. 0½d. per proof gal.
Ferrous sulphate 50 kg. 1s. 4d. kg.
Formaldehyde
40% by volume dlvd. England 1-ton lots £38 15s. ton
Glycerin
1·2627 s.g. chem. pure, 5 tons and up, 5-cwt. drums £201 10s. ton
1·2627 s.g. technical grade, 5 tons and up, 5-cwt. drums £196 10s. ton
Hexamine
1-ton lots
Technical, bulk 1s. 8d. lb.
B.P.C. 1s. 11d. „
Hydrochloric acid
Commercial 18s. 6d. cwt.
Hydrogen peroxide
27·5% weight £119 ton
35% weight £143 „
Lactic acid (1-ton lots)
Pale tech. 44% by weight 1s. 3½d. lb.
Dark tech. 44% by weight 9½d. lb.
Magnesium chloride
Solid (ex wharf): 1-ton lots £17 10s. ton
Magnesium sulphate £15 ton
Mercurous chloride (calomel)
50 kg. 65s. kg.
Mercury sulphide, red
Ton lots and over 30s. 6d. lb.
Methylated spirits (Industrial)
Perfumery quality 500 gal. and upwards: gal.
61 o.p. 7s. 4d.
74 o.p. 7s. 11½d.
5 to 10 gal.:
61 o.p. 8s. 8d.
74 o.p. 9s. 3½d.
Methyl ethyl ketone
10 tons dlvd. in drums £143 ton
Methyl isobutyl carbinol
10 tons and up, in drums, dlvd. £163 ton
Methyl isobutyl ketone
10 to 50 tons, in drums, dlvd. £169 ton
Naphthalene
Crystal, dlvd., 4-ton lots, spot £65 4s. 3d. ton
Ball and flake (ditto) £73 14s. 3d. „
Nickel sulphate
dlvd. ton lots £189 ton
Nitric acid 70% intermediate £32 „
Pentachlorphenol
Flake, technical, 1-ton lots, dlvd. 2s. 2d. lb.
Phenol Crystals:
Under 1 ton dlvd. from 1s. 7d. lb.
10 tons and over dlvd. in returnable drums from 1s. 4½d. lb.
Phthalates
10-ton lots in drums
Diethyl (B.S.) £187 10s. ton
Dimethyl (B.S.) £179 ton
Potassium bromide
50 kg. 5s. 6d. kg.
12½ kg. 5s. 8d. „
Potassium carbonate
Calcined 96 to 98% (1-ton lots ex store) £76 ton
Hydrated (1-ton lots) £74 10s. „
Potassium fluoride
28-lb. lots 5s. 1d. lb.
Potassium sodium tartrate
5-cwt. lots £10 cwt.
Soda ash
1-ton lots dlvd., from £19 16s. 6d.
Sodium cyanide
96-98% £130 ton
Sodium hydroxide 28-lb. lots:
sticks (1-lb. bottles) 4s. 3d. lb.
pellets „ „ 3s. 9d. „
Sodium metal 28-lb. lots 3s. 8d. „
Sodium metasilicate
Dlvd. U.K. in ton lots £26 ton
Sodium phosphate
Dlvd. ton lots: Di-sodium, crystalline £40 10s. ton
Anhydrous £88 „
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Anhydrous £86 „
Sodium silicate
according to quantity, grade and delivery point
8-ton lots £13 10s. ton
1-ton lots £17 „
Sodium sulphate Ex works:
(Glauber salt) £13 ton
(Salt cake) unground, full truck loads £8 16s. 6d. ton
Sodium sulphide
Broken, returnable drums, dlvd. ton lots £37 2s. 6d. ton
Flake, ditto £38 12s. 6d. „
Solid ditto £36 2s. 6d. „
Sodium sulphite
Commercial crystals 4-ton lots £24 10s. „
(Dlvd. London in 1-cwt. single non-returnable bags)
Sodium tripolyphosphate
1-ton lots £95 ton
Stannic chloride 28-lb. lots 8s. 11d. lb.
Stannous chloride 28-lb. lots 9s. 5d. lb.
Strontium carbonate
96-98% 28-lb. lots 3s. lb.
Sulphuric acid, ex-works, according to quality and quantity
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Sumatra spot £27 cwt.
Siam spot £2 7s. 6d. lb.
Candelilla Spot £23 cwt.
Carnauba
Prime, Spot £48 cwt.
Fatty grey £29 „
Gum arabic Lump £7 5s. cwt.
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Paraffin wax
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Peru balsam 11s. lb.
Shellac
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No. 2 orange £11 10s. „
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Pale dewaxed 6s. „
Tragacanth
No. 1 spot £127 10s. cwt.
No. 2 spot £121 „
Pale leaf £50 „
Amber £36 „
Brown to Red £27 „

NEW PATENTS

COMPLETE SPECIFICATIONS ACCEPTED

Steroids

Purification of esters of hecogenin. *Glaxo Laboratories Ltd.* 811,134.

Steroids and the manufacture thereof. *Upjohn Co.* 809,820; 810,858; 810,859.

Dehydro-compounds of the steroid series and process of making same. *Organon Laboratories Ltd.* 811,867.

Steroid compounds. *Soc. des Usines Chimiques Rhône-Poulenc.* 811,205

Hydroxy-steroids and process for their manufacture. *Ciba Ltd.* 811,845.

Process for the preparation of enol esters from ketosteroid compounds. *Organon Laboratories Ltd.* 811,531.

Manufacture of a 17-hydroxysteroid. *Farbwerke Hoechst Aktiengesellschaft Vorm. Meister, Lucius, and Brüning.* 810,264.

Biologically active steroid compounds and process for the preparation thereof. *Organon Laboratories Ltd.* 811,961.

Preparation of steroid compounds. *Glaxo Laboratories Ltd.* 811,632.

Salts of oestrone sulphate and the manufacture thereof. *Schering A.G.* 810,917.

Steroid compounds and a process for their preparation. *Organon Laboratories Ltd.* 811,901.

Dyestuffs

Water-insoluble quinazoline monoazo dyestuffs. *Farbenfabriken Bayer A.G.* 811,953.

Stilbene monoazodyestuffs and process for their manufacture. *Ciba Ltd.* 810,297.

Water-insoluble diphenylamine dyestuffs. *Sandoz Ltd.* 810,360.

Metal-containing tricyclic chelating monoazo dyestuffs and their use. *Geigy A.G.* 812,151.

Disazo dyestuffs derived from sulphonates. *Farbenfabriken Bayer A.G.* 810,246.

Metalliferous complexes of mono-azo dyestuffs of the acylacetic amide series, and their preparation. *Compagnie Française des Matières Colorantes.* 810,207.

Monoazo dyestuffs of the benzeno-azo-naphthalene series and metal complexes thereof. *General Aniline and Film Corp.* 811,521.

Antibiotics

Production of an antibiotic designated antibiotic 101a by fermentation. *Upjohn Co.* 811,757.

Production of chloramphenicol and similar compounds. *P. May (C. F. Boehringer and Soehne G.m.b.H.)* 811,846.

Culture medium for the production of spiramycin by fermentation. *Soc. des Usines Chimiques Rhône-Poulenc.* 811,971.

Penicillin salts of aminoguanidines. *Imperial Chemical Industries Ltd.* 810,569.

Penicillin compounds and intermediates for use in their production. *Leo Industrie Chimiche Farmaceutiche.* 810,518.

Pharmaceuticals and fine chemicals

Pyrrolidine derivatives and a process for the manufacture thereof. *Hoffmann-La Roche and Co. A.G.* 811,698.

Aromatic esters and pharmaceutical preparations containing them. *Ciba Ltd.* 812,360.

2 - Hydroxy - 4 - arylaminoquinolines. *Geigy A.G.* 811,957.

Indole derivatives. *Imperial Chemical Industries Ltd.* 809,691.

3-Substituted indoles. *Upjohn Co.* 809,795.

Cyclopentanophenanthrene compounds. *Laboratoires Français de Chimiotherapie.* 810,009.

Therapeutically valuable esters of 3 : 5 : 5-trimethylcyclohexanol and mandelic acid, and a process for the preparation thereof. *Koninklijke Pharmaceutische Fabrieken Voorheen Brocades-Stheeman and Pharmacia N.V.* 810,888.

Process for the production of 1 : 2-diphenyl - 4 - *N* - butyl - 3 : 5 - dioxopyrazolidine. *Geigy A.G.* 812,449.

Method of extracting and purifying a pancreatic hormone acting on the respiratory centres. *J. P. D. Santenoise.* 810,204.

Pharmacologically active piperazine derivatives and processes for preparing them. *Laboratoria Pharmaceutica Dr. C. Janssen N.V.* 809,760.

β - Thio - substituted acylamino-nitropropiophenones and process for the preparation thereof. *Farmaceutici Italia S.A.* 809,794.

Active substance from plants of the Rauwolfia species and process for manufacturing same. *Ciba Ltd.* 809,912.

Process for the manufacture of morphinane and morphinane derivatives. *Hoffman-La Roche and Co. A.G.* 811,689.

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APPLICATIONS

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FARACO.—779,286. *T. H. Jacobs.*

QUIBON.—779,319. *Hormo-Pharma (Sales) Ltd.*

CATAPRESAN. — 779,805. *C. H. Boehringer Sohn.*

SALIGEX.—780,539. *Macleans Ltd.*

RANDOLECTIL.—780,646. *Farbenfabriken Bayer A.G.*

COLBAX.—782,098. *Letchworth Pharmaceuticals Ltd.*

EVENTIN.—782,869. *Knoll A.G.*

ACTOMOL.—782,422. *Imperial Chemical Industries Ltd.*

FILIBON.—777,094. *American Cyanamid Co.*

TRACTOPAN.—779,103. *Bayer Products Ltd.*

ANTURAN.—779,442. *J. R. Geigy S.A.*

PARABAL.—779,781. *West Pharmaceutical Co. Ltd.*

DELFEN.—780,840. *Ortho Pharmaceutical Corp.*

ASTRACAINE.—780,948. *A/B Astra, Apotekarnes Kemiska Fabriker.*

SYNAPROL.—781,784. *Farbenfabriken Bayer A.G.*

ADROMIN.—782,338. *Glaxo Laboratories Ltd.*

ANCOMYCETIN. — 767,099. *Mesco Laboratories Ltd.*

QUARZAN.—776,491. *Roche Products Ltd.*

VIE D'OR.—778,253. *H. and T. Kirby and Co. Ltd.*

SANTARAX.—778,259. *A/B Pharmacia.*

SOMNOTIL.—778,416. *Allied Laboratories Ltd.*

CONSOL.—778,838. *Austin Ibison.*

RHINODIL.—779,730. *Allied Laboratories Ltd.*

NERSPRIN.—780,673. *J. Waterhouse and Co. Ltd.*

MALLPAS.—B781,536. *Mallpas (Pharmaceuticals) Ltd.*

MYLODEX.—781,901. *Brook Parker and Co. Ltd.*

POLARITON.—781,903. *Allen and Hanburys Ltd.*

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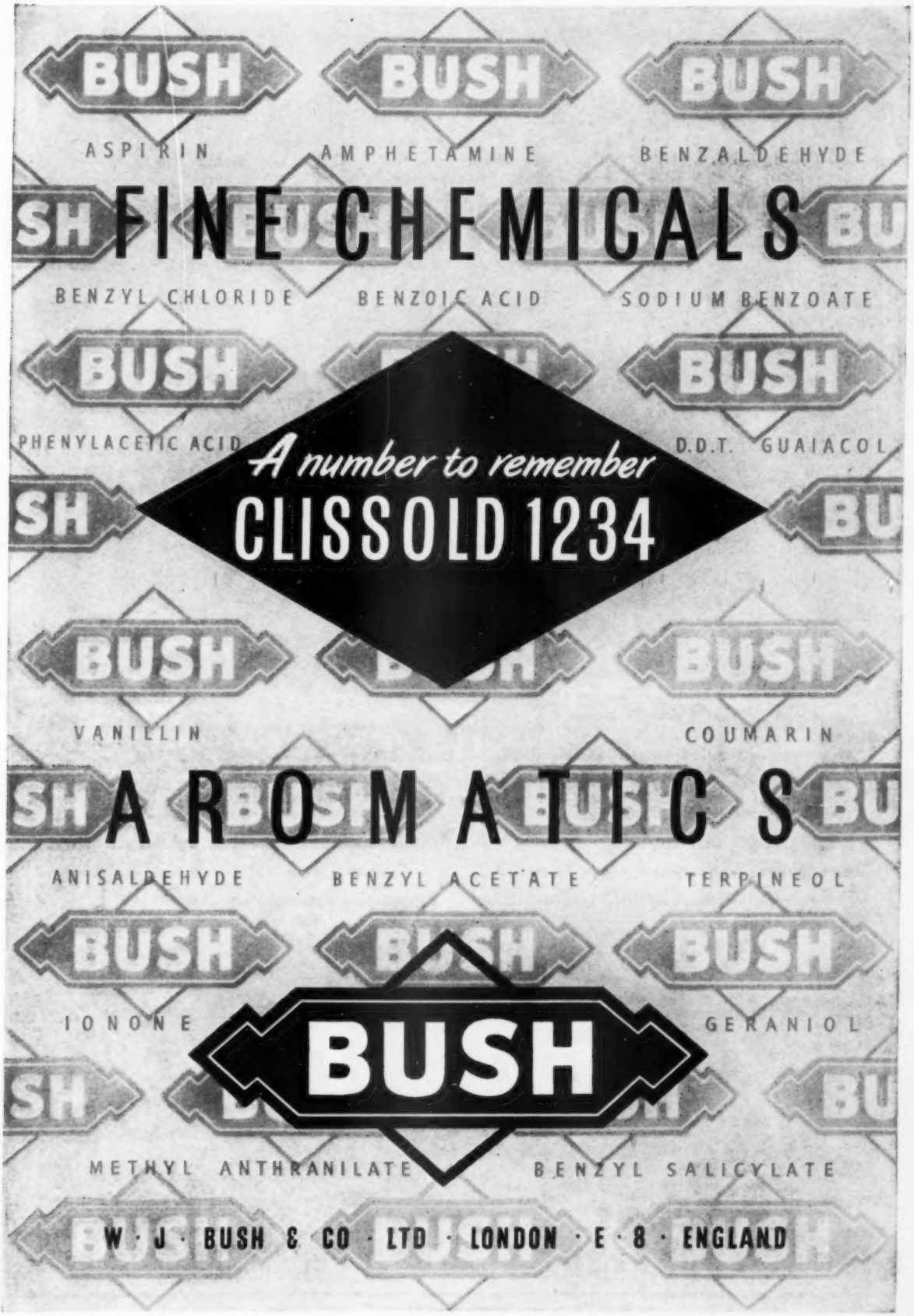
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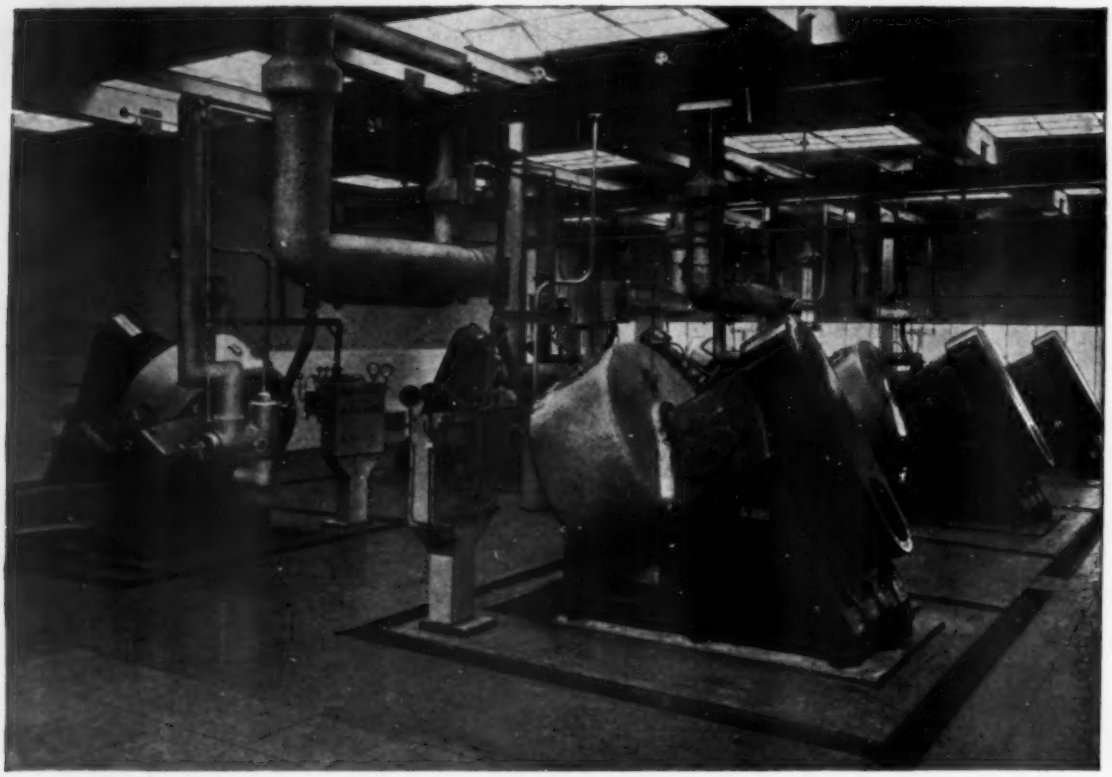

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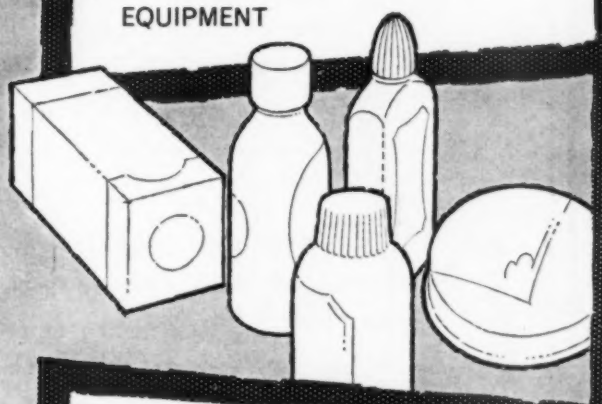

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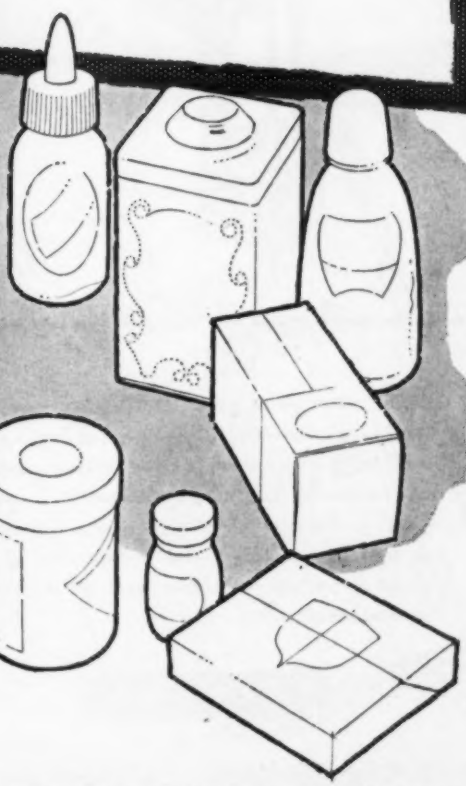

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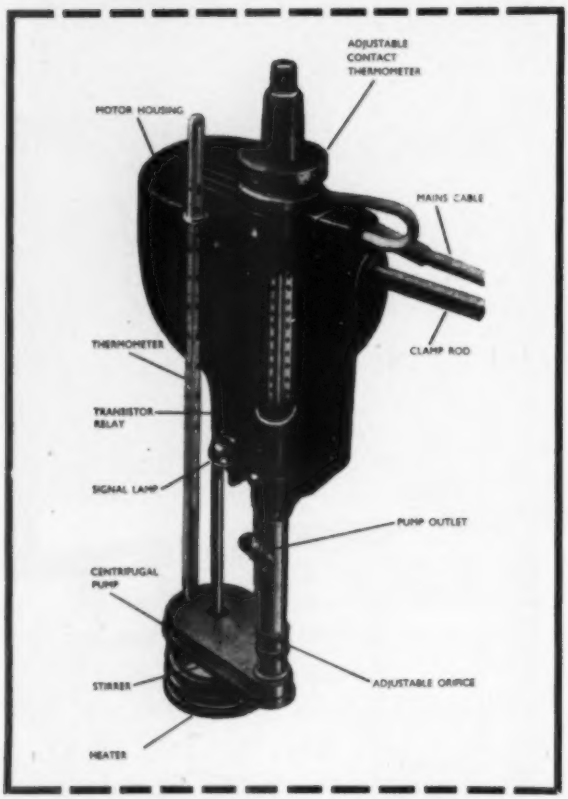

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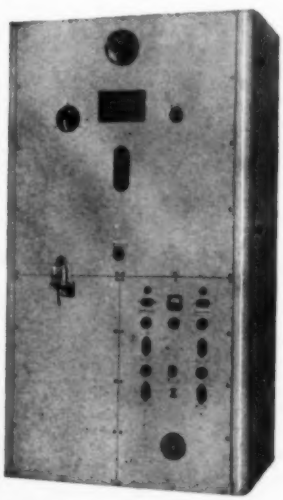

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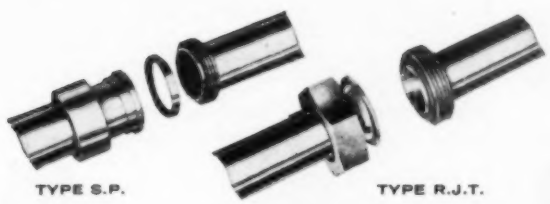

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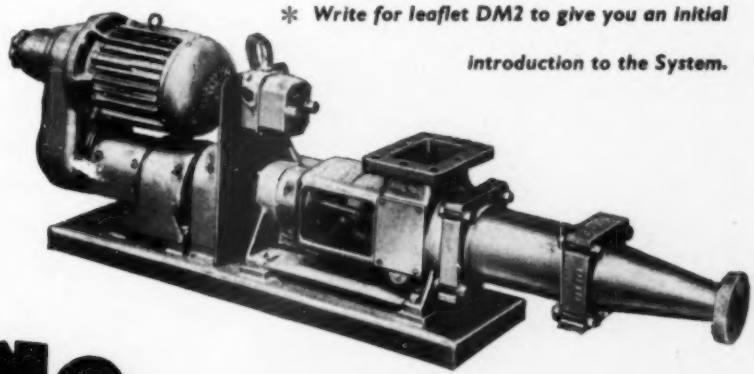

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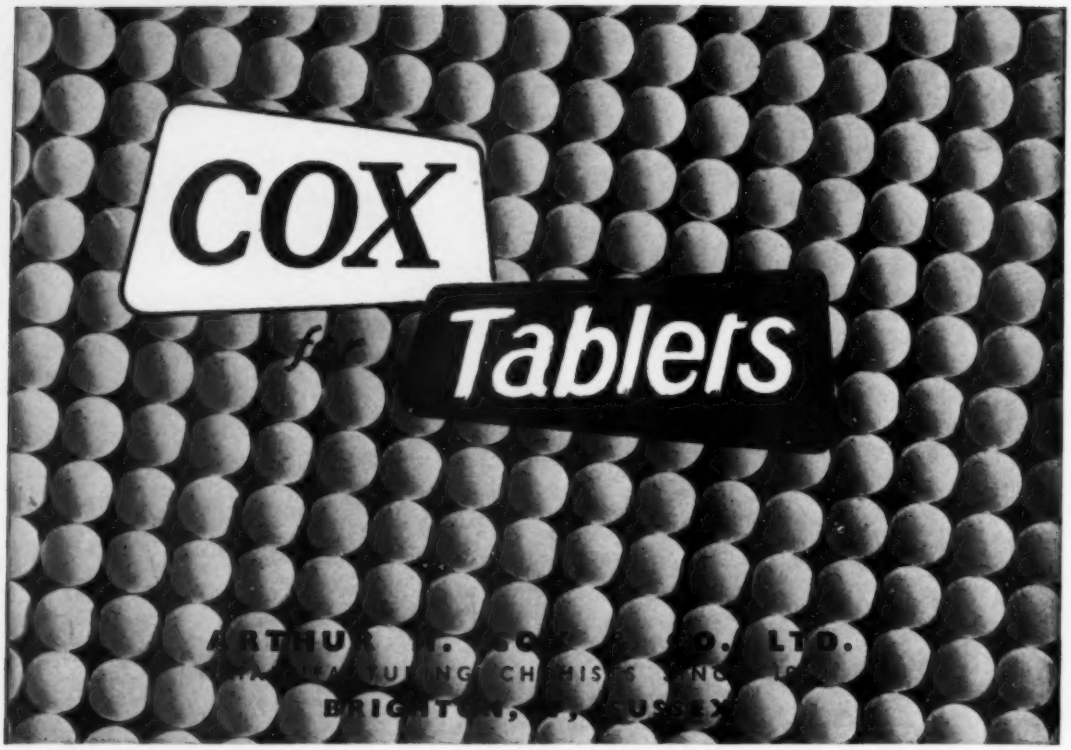

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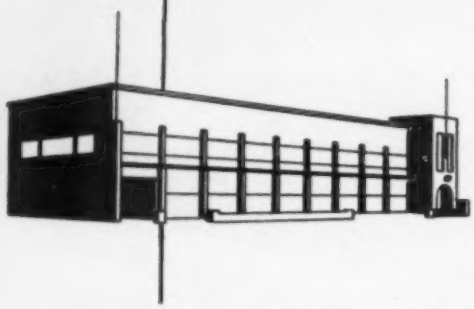

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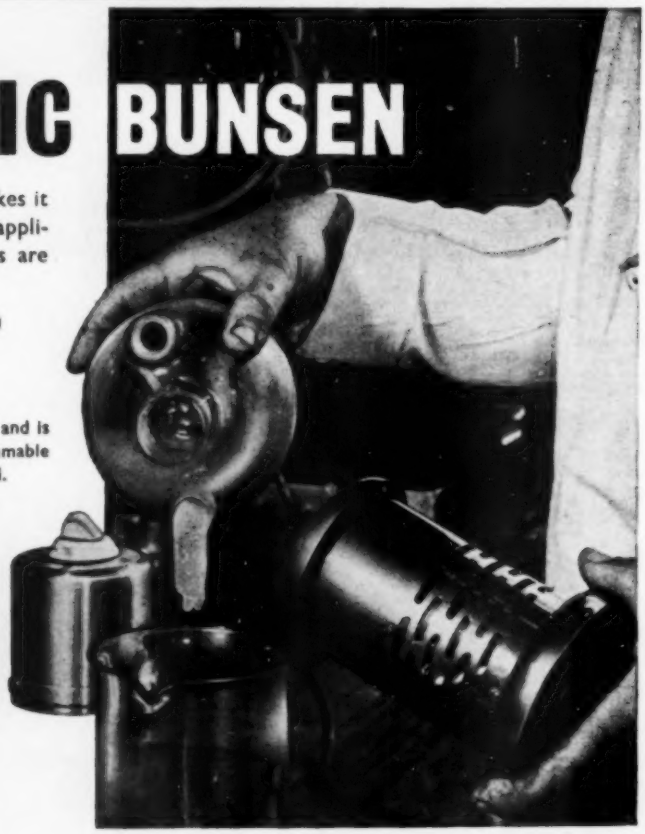

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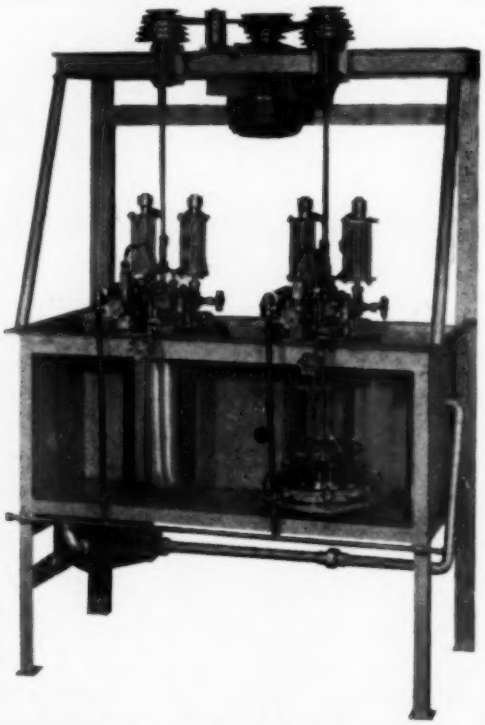

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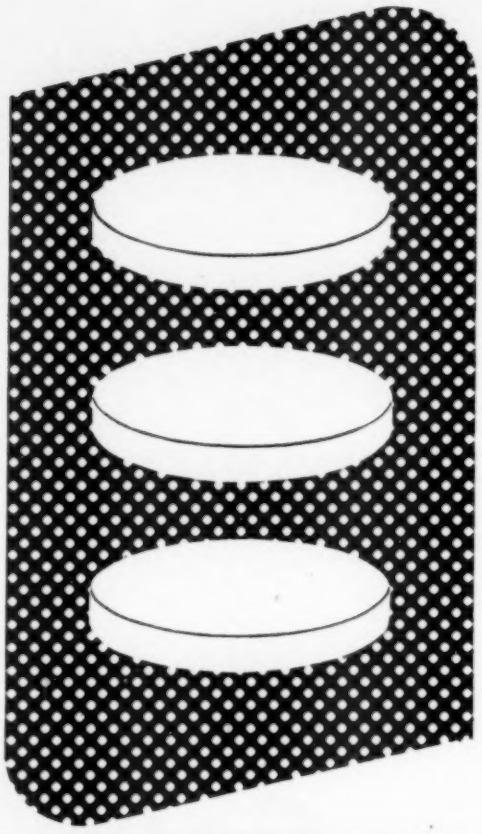

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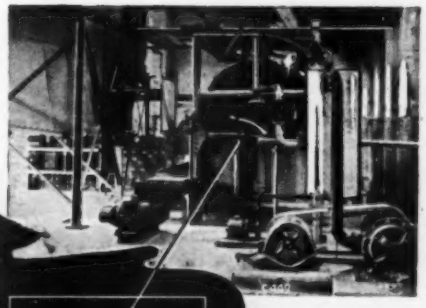

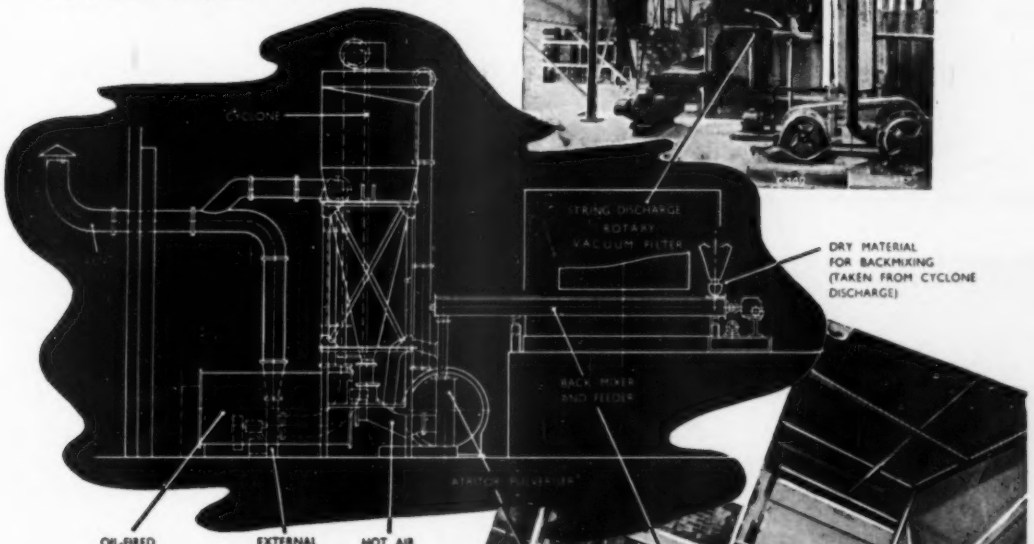

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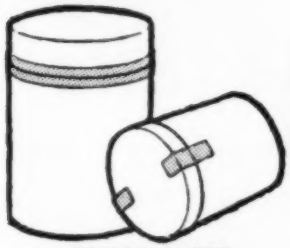

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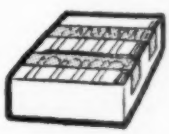

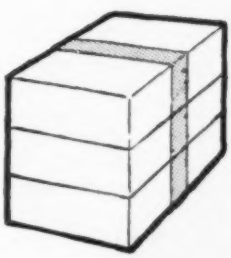

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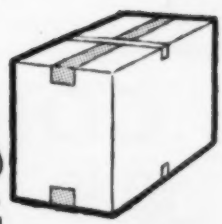

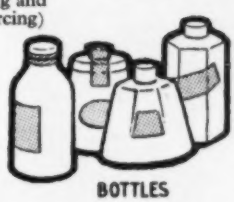

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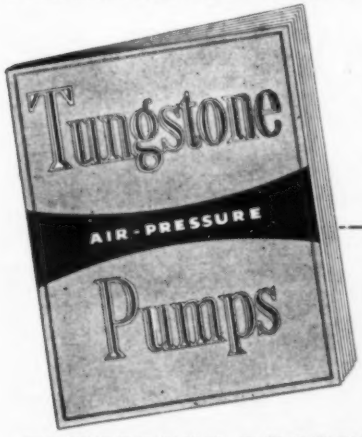

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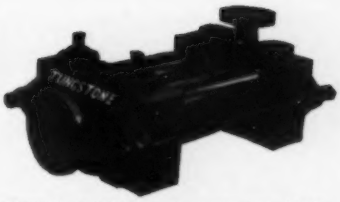

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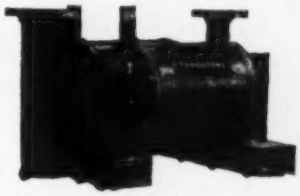

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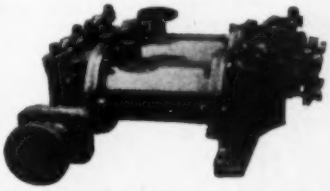

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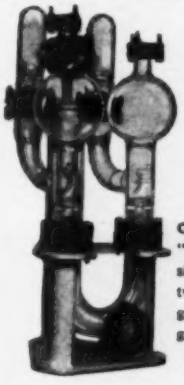

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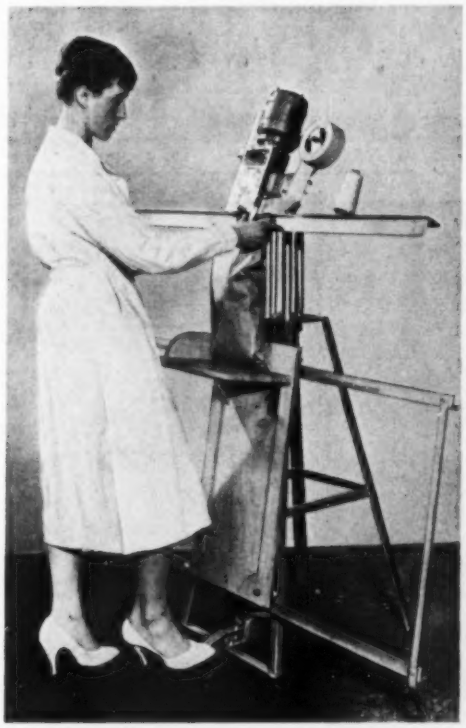

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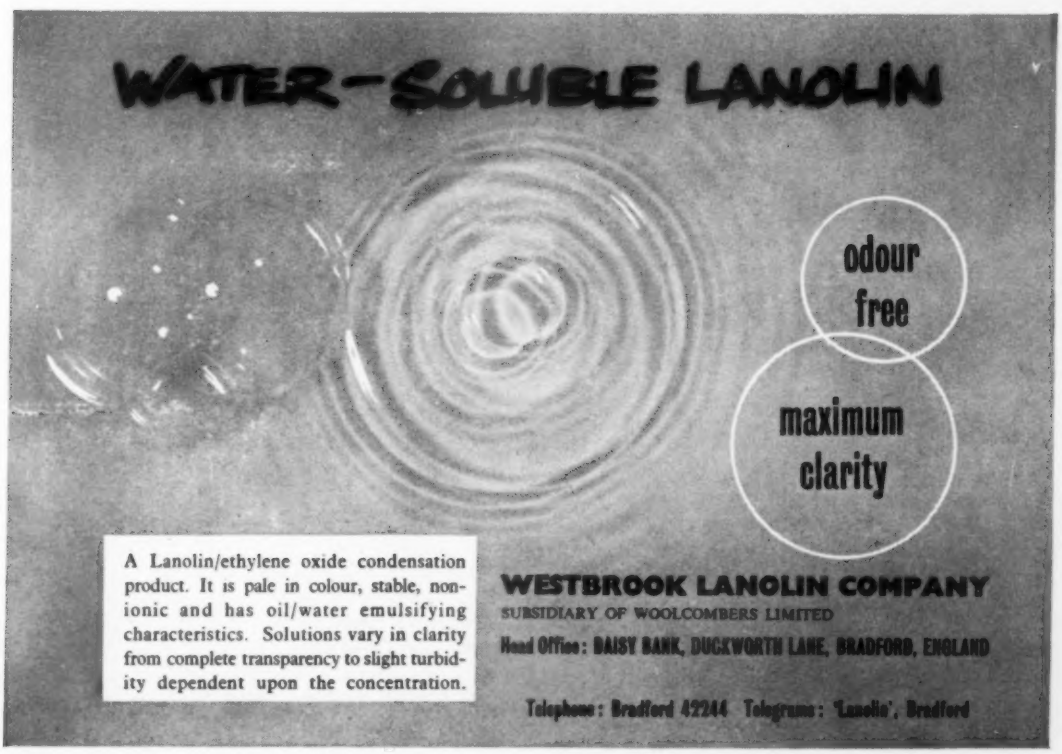
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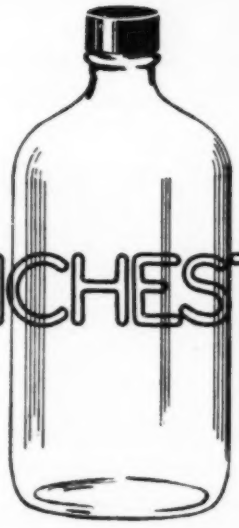

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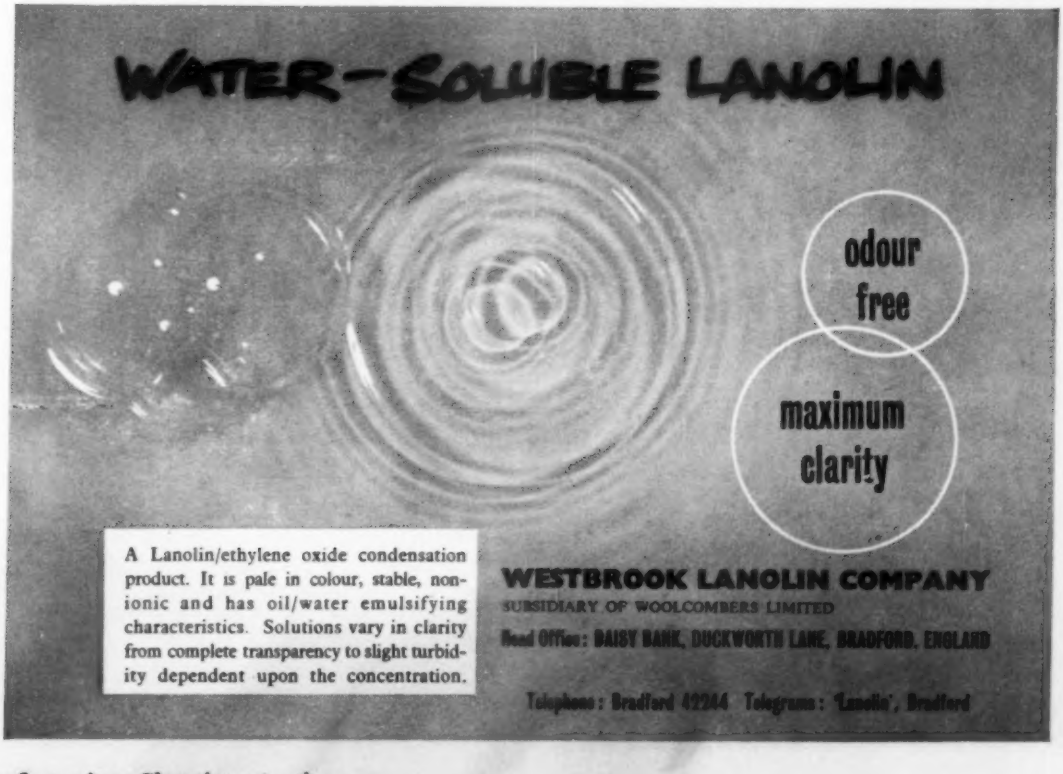
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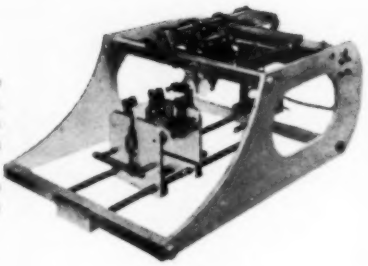

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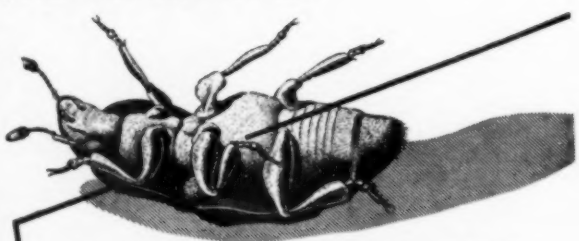

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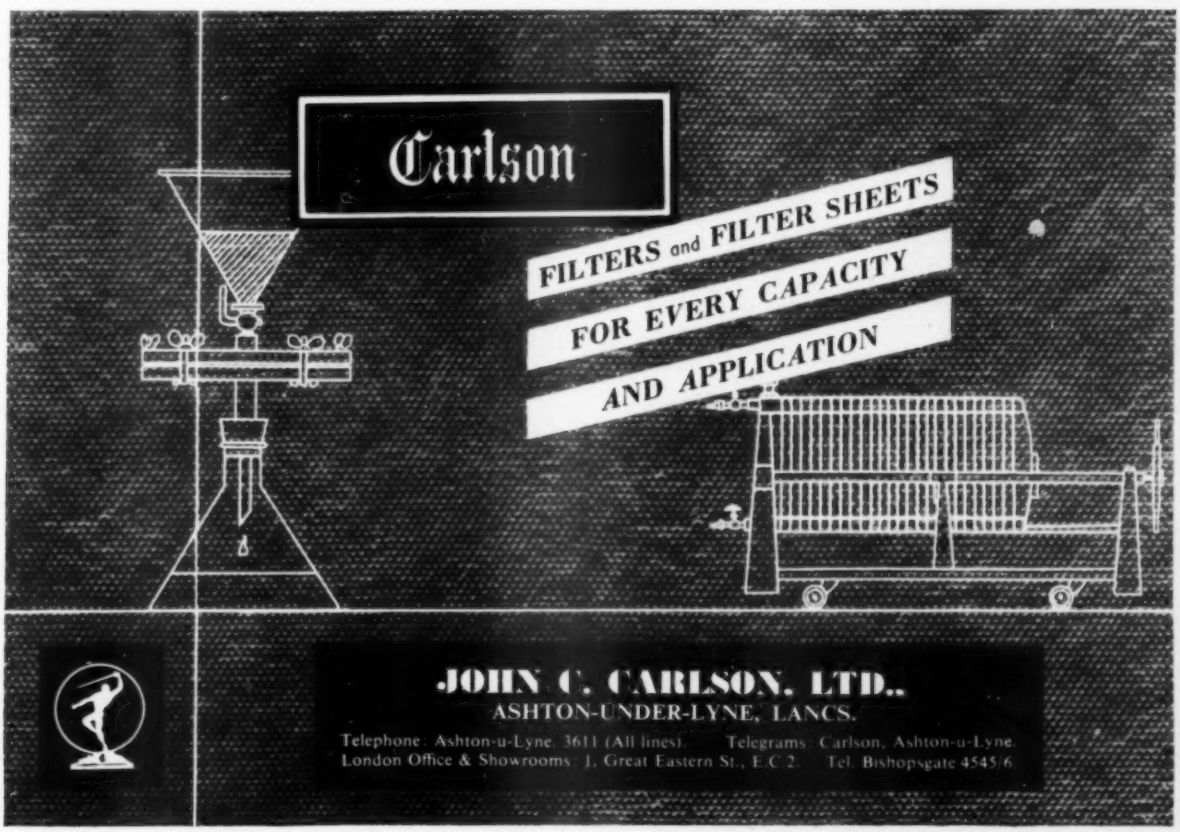
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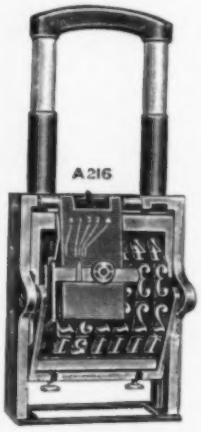

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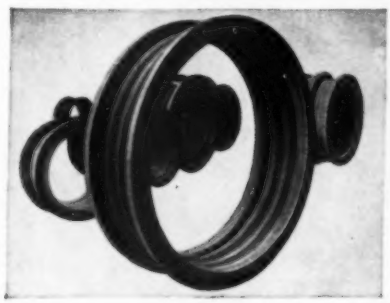

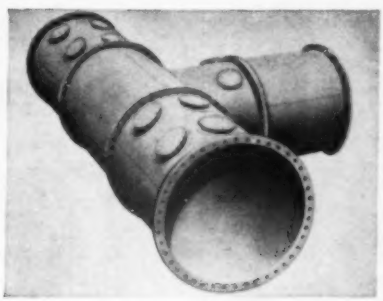

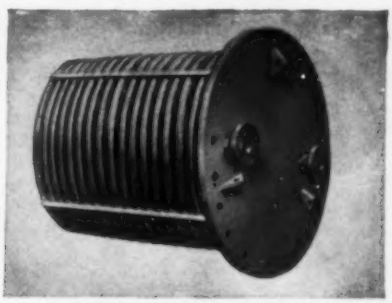

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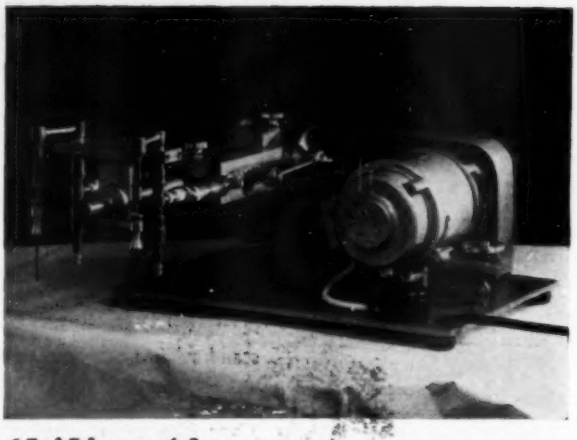

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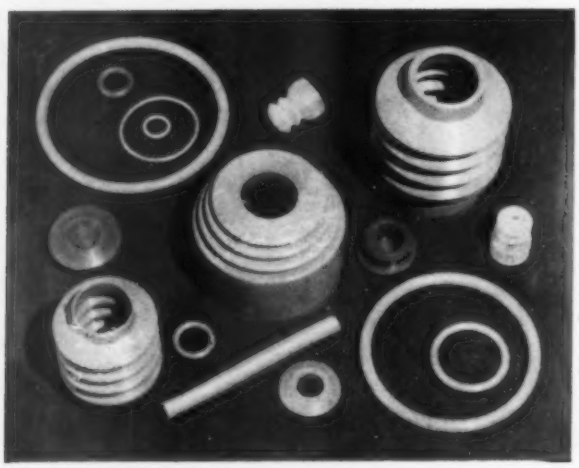

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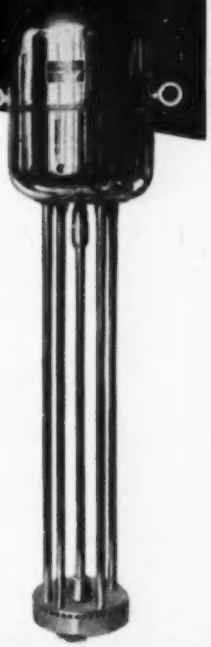

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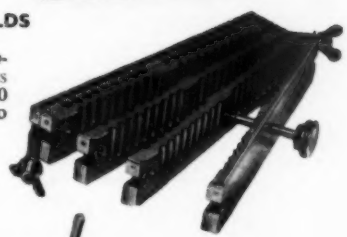

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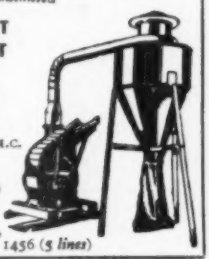

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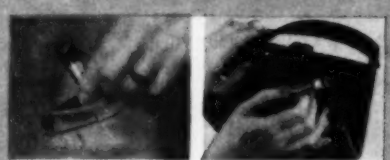

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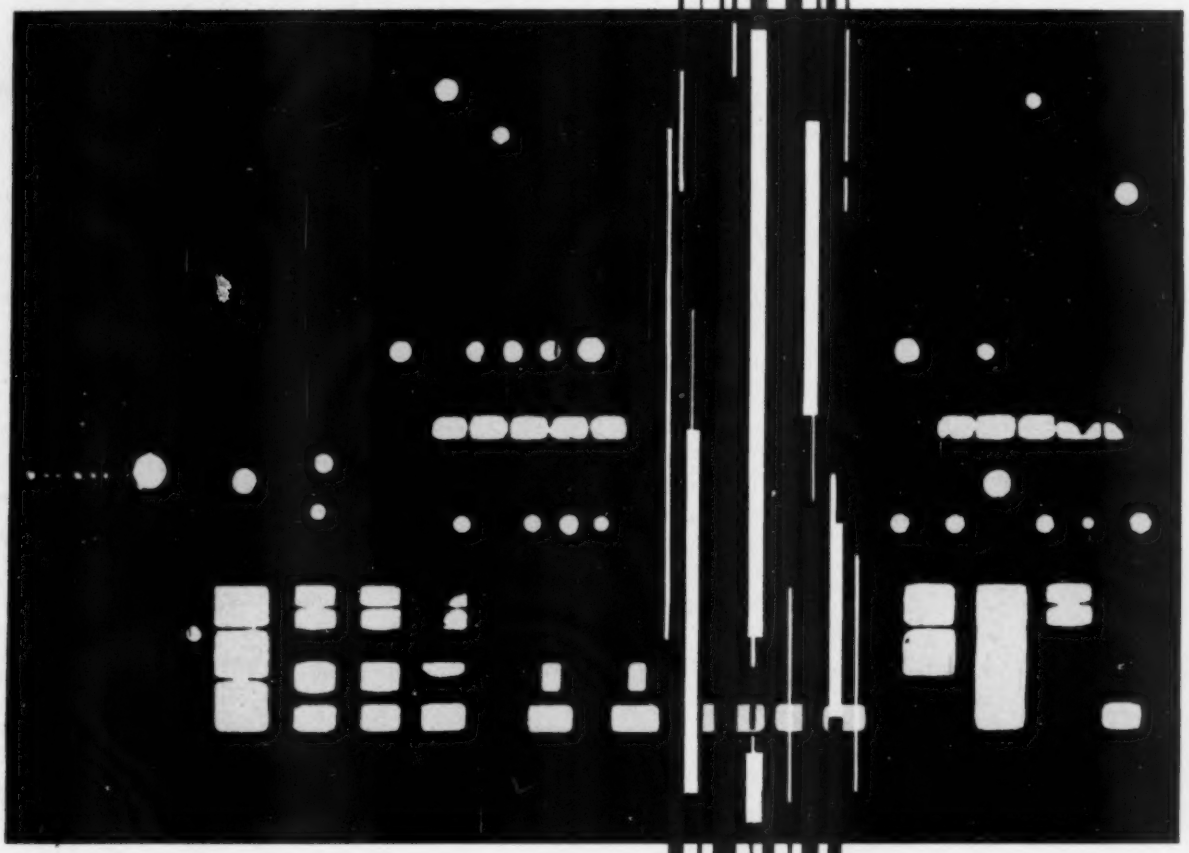

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